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AN EXPERIMENTAL STUDY OF HYPER-NEUROTIZATION *

BYRON STOOKEY, A.M., M.D.

NEW YORK

Neurotization of paralyzed muscle by direct implantation of a mixed nerve has been amply proved, both experimentally and clinically. This procedure has formed, in part, the basis of a new method whereby artificial nerve branches may be added to a nerve trunk and paralyzed muscle neurotized when the distal end of the artificial branch is implanted into the muscle.[1] However the problem here studied is not, Can muscle without nerve supply be thus neurotized? but, Can muscle having its normal innervation be made to take on an additional and foreign nerve when such methods of direct nerve implantation are utilized? For example, Can the biceps muscle be innervated by the musculocutaneous and also, at the same time, by the ulnar nerve? a problem perhaps of less clinical application than of biologic significance.

Erlacher,[2] in 1914, obtained hyperneurotization, but Steindler,[3] in 1916, and others failed to find evidence to indicate that increased neurotization was possible. The histologic evidence offered by Erlacher in favor of hyperneurotization was susceptible to question, since the method used to differentiate the motor end plates and fibers of the normal musculocutaneous from those of the implanted median or ulnar nerve relied essentially on differences in size of the fibers and depth with which the motor end plates and nerve fibers took up the

* From the Laboratory of Experimental Neurology, College of Physicians and Surgeons, Columbia University.

* Read before the Forty-Ninth Annual Meeting of the American Neurological Association, Boston, May 31, 1923.

1. Stookey, Byron: Artificial Nerve Branches for Innervation of Paralyzed Muscles, Arch. Surg. **6**:731 (May) 1923.

2. Erlacher, P.: Hyperneurotisation; muskuläre Neurotisation; freie Muskeltransplantation; experimentelle Untersuchungen, Zentralbl. f. Chir. **41**: 625 (April) 1914. Ueber die motorischen Nervenendigungen. Histologische und experimentelle Beiträge zu den Operationen an den peripheren Nerven, Ztschr. f. orthop. Chir. **34**:561, 1914.

3. Steindler, A.: Direct Neurotization of Paralyzed Muscles; Further Study of the Question of Direct Nerve Implantation, Am. J. Orthop. Surg. **14**:707 (Dec.) 1916.

stain. It is well known that, normally, relatively wide variations are found in the depth with which nerve fibers stain. In the same specimen such variations occur that differentiation of old from new fibers is misleading when the criteria to distinguish them is based on such slight differences in staining. That such differences do not offer adequate means of differentiation has been emphasized by the more recent knowledge that both spinal and sympathetic fibers as well as their motor end plates are found in striate muscle. The fibers and end plates of these two systems may show marked differences in size and staining variations. Even by serial section it is doubtful if nerve fibers or motor end plates may be satisfactorily traced back to their origin and identified as derived from one or the other of the nerves concerned. Only by cutting one or the other of the nerves and allowing degeneration to take place can conclusive evidence as to the origin of certain nerve fibers be deduced. In this series of experiments twenty-one rabbits were used; two died and were lost to the experiment. In the remaining nineteen, hyperneurotization was obtained in all with one exception. In the first animal operated on, the implanted nerve was found 365 days later, free in the tissues with a slight bulb on its end: apparently the implantation had not held.

TECHNIC EMPLOYED

In these experiments the ulnar nerve was cut and implanted into the biceps without disturbing the musculocutaneous nerve. The technic of implantation is simple. Very fine, split, waxed silk was passed through the epineurium of the ulnar nerve, care being taken to avoid injury to the cut end. The sutures were then carried into the depths of a slit made in the biceps muscle (See Fig. 1). The direction of the implanted nerve was parallel to the muscle fibers. After implantation, the opening in the muscle was closed and the wound sutured in layers. After various periods the animals were then investigated, both for physiologic and histologic evidence of hyperneurotization.

PHYSIOLOGIC EVIDENCE OF HYPERNEUROTIZATION

At intervals varying from 120 to 856 days the biceps was exposed aseptically, examined, and electric stimulations were made and muscle tracings obtained.

Tracings were obtained first by stimulation of the musculocutaneous and then the ulnar nerve. In each experiment contraction of the biceps occurred on stimulation of either the normal musculocutaneous or the implanted ulnar. After responses from both nerves had been recorded, the musculocutaneous nerve was cut. To prevent outgrowth into the biceps from the cut end the nerve was tied and implanted into the pectoralis major muscle. Thus the musculocutaneous innervation to the

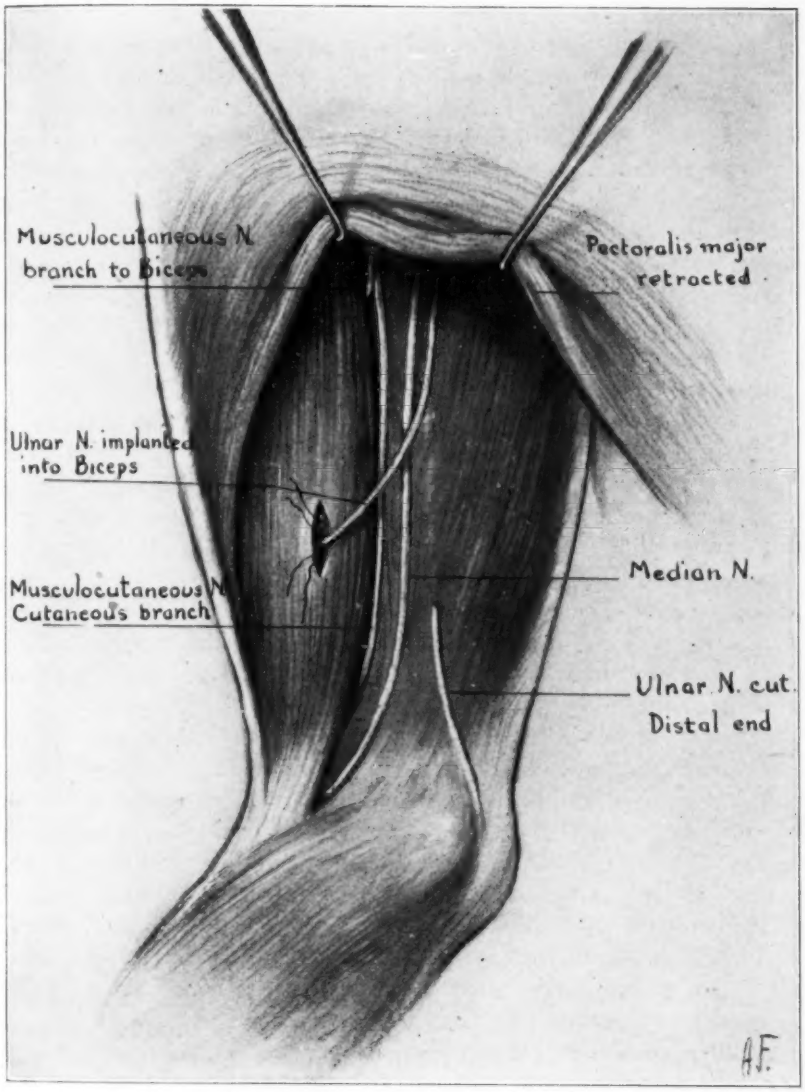

Fig. 1.—To illustrate technic of hyperneurotization. The musculocutaneous branch to the biceps muscle is left intact and the cut central end of the ulnar nerve implanted into the biceps.

biceps was destroyed to rule out the possibility of dispersion or spread of the current along the implanted ulnar nerve to normal motor end plates of the musculocutaneous. It had been considered possible that the implanted ulnar might serve in the muscle as a passive conductor of the current to fibers or end plates of the musculocutaneous without having formed actual functional motor end plates of its own, and that contraction might be obtained through the musculocutaneous end plates. Such contractions might erroneously be attributed to functional end plates of the ulnar nerve. But if, on stimulation of the ulnar contraction of the biceps could be obtained after the musculocutaneous nerve had been cut—sufficient time being allowed to elapse for its end plates to degenerate, yet not long enough for neurotization to take place from the implanted ulnar—hyperneurotization could be proved.

At intervals of from ninety-six hours to thirty-two days after cutting the musculocutaneous nerve the rabbits were killed and tracings obtained of the biceps contractions produced by stimulation of the ulnar nerve. In all these experiments contraction of the biceps took place. Stimulations of the musculocutaneous and the adjacent nerves were also made to rule out downgrowth from the musculocutaneous and reinnervation of the biceps by this nerve, and also to exclude the presence of aberrant branches to the biceps from adjacent nerves. In no case did the biceps respond except on stimulation of the implanted ulnar, thus showing that regeneration of the musculocutaneous had not taken place and that the biceps did not receive aberrant branches from any other nerve (Fig. 2).

Tracings showing contraction of the biceps on stimulation of the musculocutaneous and ulnar nerves were thus obtained: first, when both of these supplied the muscle, and again at a later period, after the musculocutaneous had been cut, when the implanted ulnar was its only supply. From a physiologic standpoint the electric responses thus recorded prove that hyperneurotization of the biceps had taken place.

However the nature of the contraction differed in that the response obtained from the normal muculocutaneous was always greater than that from the implanted ulnar. Furthermore, in some instances the contraction of the biceps on ulnar stimulation was quick, but frequently appeared to be limited and did not include all of the muscle.

HISTOLOGIC EVIDENCE OF HYPERNEUROTIZATION

Even though fairly conclusive physiologic evidence of hyperneurotization had been found, it was felt that perhaps the problem would be more completely solved if histologic, as well as physiologic, proof were obtained. As has been said, neither serial sections nor variations in the depth with which the nerve fibers take up the stain

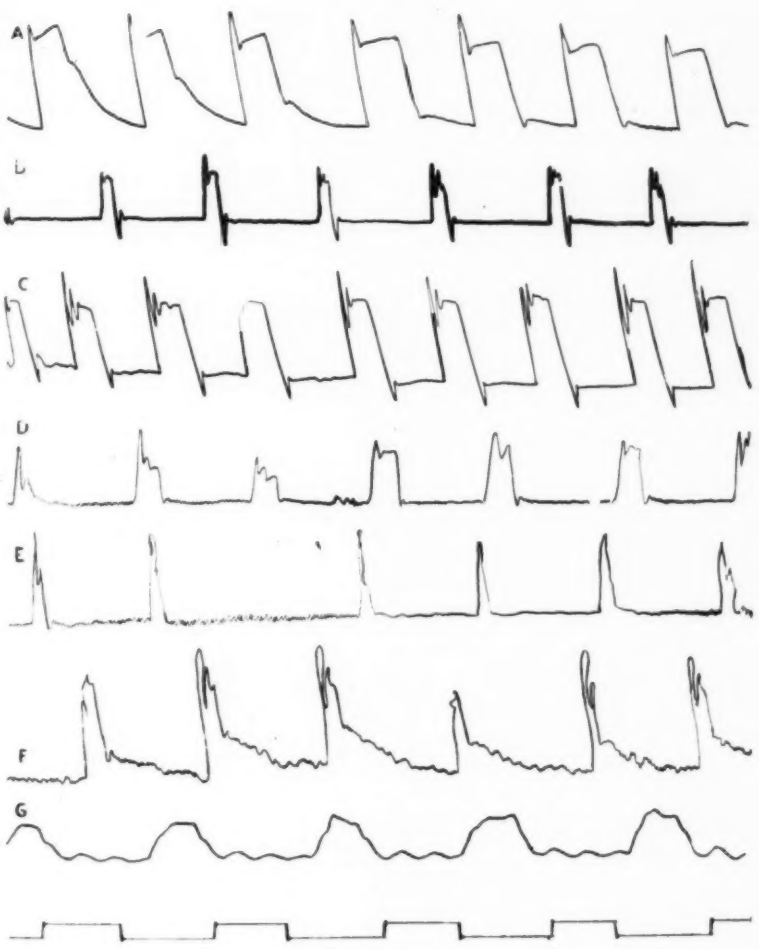

Fig. 2 Rabbit 68: Ulnar nerve implanted into biceps 140 days earlier; musculocutaneous nerve left intact; *A*, contraction of biceps on stimulation of musculocutaneous nerve; *B*, contraction of biceps on stimulation of ulnar immediately after musculocutaneous nerve was cut.

Rabbit 67: Ulnar nerve implanted into biceps 163 days earlier; musculocutaneous left intact. *C*, contraction of biceps on stimulation of ulnar nerve, thirty-two days after musculocutaneous was cut. Before cutting musculocutaneous, contraction of biceps was obtained on stimulating either nerve.

Rabbit 57: Ulnar nerve implanted into biceps 557 days earlier; musculocutaneous nerve left intact. Before cutting the musculocutaneous, contraction was obtained on stimulating both musculocutaneous, *D*, and ulnar nerves, *E*. *F*, contraction of biceps on stimulation of ulnar nerve seven days after musculocutaneous was cut.

Rabbit 59: Ulnar nerve implanted into biceps 864 days earlier; musculocutaneous nerve left intact. *G*, contraction of biceps on stimulation of ulnar nerve ninety-six hours after musculocutaneous nerve was cut.

is a satisfactory histologic method to differentiate, in the same muscle, nerve fibers and motor end plates of the musculocutaneous nerve from those of the implanted nerve. However, this histologic differentiation could be made if the musculocutaneous nerve were cut, and sufficient

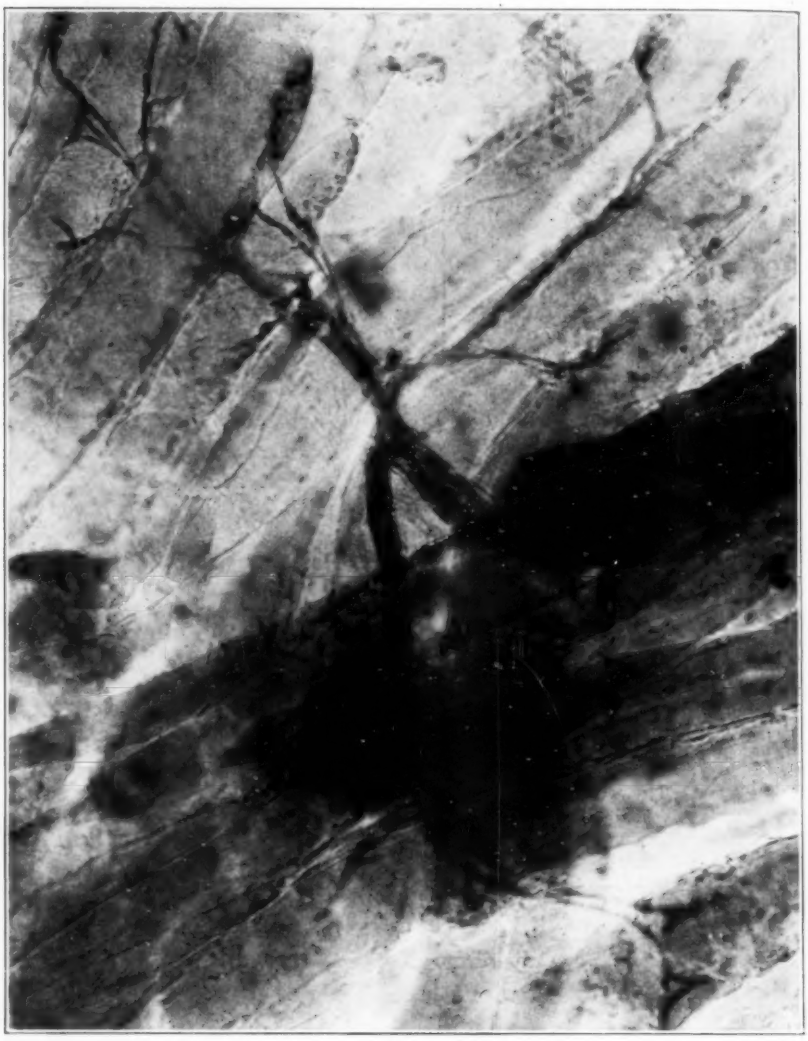

Fig. 3.—Motor-end plate in hyperneurotized biceps muscle. Stohr's gold chlorid stain; teased specimen. Low power.

time allowed to elapse for degeneration of its nerve fibers and motor end plates to take place. The biceps muscle into which the ulnar nerve had been implanted could then be studied by appropriate staining measures

for normal appearing nerve fibers and motor end plates. If normal motor end plates were found after the musculocutaneous nerve had been cut, histologic evidence of hyperneurotization would then be available. Under such experimental circumstances normal motor end plates may be accepted as coming from the implanted ulnar nerve, since it is the only remaining nerve that on stimulation caused contraction of the biceps—all other neural connection with the biceps having been ruled out by electric stimulation.

Fig. 4.—Motor-end plate in hyperneurotized biceps muscle. Stohr's gold chlorid stain, teased specimen. High power. Note that the muscle fibers are of normal and uniform size and show normal striations.

The biceps muscle thus obtained was stained by Stohr's gold chlorid method and teased specimens were examined [4] (Figs. 3 and 4). Numerous normal appearing motor end plates and nerve fibers were to be seen scattered throughout the muscle. The muscle fibers appeared

4. I wish to take this opportunity to express my appreciation to Dr. Oliver S. Strong for staining these sections.

to be of normal and uniform size, which is further evidence that degeneration of the muscle fibers had not taken place in spite of the fact that sufficient time had elapsed in some of the series for muscle changes to be present. Grossly, the biceps muscle appeared normal in color even in those specimens in which the musculocutaneous nerve had been cut thirty-two days previously. If in these cases the biceps had not been innervated by the ulnar, degeneration of the muscle fibers would have been apparent. Neither fibrillation nor alteration in color of the muscle were noted in any of the experiments, though the time between cutting the musculocutaneous and examination of the muscle varied from ninety-six hours to thirty-two days. Thus the macroscopic appearance of the muscle may be taken as further confirmation of the histologic and physiologic findings.

CONCLUSIONS

(1) After implantation of the ulnar nerve into the biceps muscle, still possessing its normal innervation, contraction of the biceps was obtained on stimulation of either the ulnar or the musculocutaneous nerves.

(2) Contraction of the biceps occurred on stimulation of the ulnar nerve immediately after the musculocutaneous had been cut and at various intervals thereafter, showing that the stimulation could not be attributed to dispersion of the current from the ulnar fibers in the muscle to the motor end plates of the musculocutaneous, but to functional end plates of the ulnar nerve.

(3 After cutting the musculocutaneous nerve and before regeneration of the musculocutaneous could take place, normal motor end plates were found by histologic methods, which electrical examination showed could be derived only fro mthe implanted ulnar nerve.

(4) Thus both the physiologic findings and the evidence obtained by histologic degenerative methods permit one to conclude that hyperneurotization of normal muscle is possible.

DISCUSSION

DR. ERNEST SACHS, St. Louis: Some years ago the late Dr. Halsted pointed out that a gland would not grow when implanted in an animal in which that gland was present. I wonder whether there is any comparison to be made between this condition and the experiments of Dr. Stookey; whether such gland experiments could be applied to the situation here. If they could, it would distinctly contradict that view. Has Dr. Stookey thought of it from that standpoint? Applying Dr. Halsted's views, the muscle should not get a new nerve supply since there is an adequate nerve supply already.

DR. STOOKEY: I share the view of Dr. Sachs that, biologically, this feature should be expected. When this work was begun it was with the expectation of disproving the existence of hyperneurotization and the results were unexpected.

BRAIN CHANGES IN TYPHUS FEVER CONTRASTED WITH THOSE IN EPIDEMIC ENCEPHALITIS AND ACUTE POLIOMYELITIS *

G. B. HASSIN, M.D.
Associate Professor of Neurology, College of Medicine,
University of Illinois
CHICAGO

Recent pathologic studies of typhus fever, especially by German and Russian workers, have shown that in this disease the nervous system is not only involved with remarkable constancy, but is even involved more than any other part of the body. Because of the rarity of typhus in this country, American contributions on its pathology in general and that of the nervous system in particular are lacking. To Dr. J. Tarassewitz of Moscow, Russia, I am indebted for the brain of one case, and to Dr. E. K. Piette of Kharkov, Russia, for a number of paraffin blocks from two cases of typhus fever. In addition, I had the opportunity, during my stay in Russia last year, to study a number of stained sections and to secure a number of valuable contributions in the Russian language.[1]

As the brain changes in typhus fever are those of an acute encephalitis, it seemed desirable to contrast them with the epidemic and poliomyelitic types.

MACROSCOPIC AND MICROSCOPIC FINDINGS

The brain showed no striking macroscopic changes. They were absent also in one hundred cases studied by Nicol.[2]

Nodules.—Under the microscope, changes were abundant. Most noteworthy were the so-called nodules or granulomas, that were present in the cortex, basal ganglia, midbrain, medulla, cerebellum and spinal cord. I found none in the meninges or the choroid plexus where their presence has been affirmed by Ceelen.[3] They appeared as compact roundish or ovoid bodies (Fig. 1) and consisted of cellular elements which showed as pale nuclei, rod-like, horse-shoe, oblong or curved

* From the Division of Neurology of the College of Medicine of the University of Illinois and the Pathology Laboratories of the Illinois State Psychopathic Institute and Cook County Hospital.

1. Some have been reviewed by Dr. Peter Bassoe in the Practical Medicine Series, Nervous and Mental Diseases, Vol. 8, Series 1922, p. 171.

2. Nicol, Kurt: Pathologisch-anatomische Studien beim Fleckfieber, Beitr. z. path. Anat. **65**:120, 1919.

3. Ceelen, W.: Die pathologische Anatomie des Fleckfiebers, Ergeb. d. allg. Path. u. path. Anat. **19**:313, 1919.

in shape (Fig. 2). These multiform cell nuclei contained very few granules of chromatin; in suitably stained specimens (Alzheimer-Mann), they showed a certain amount of cytoplasm. In the center of the nodules the cells were more densely packed than at the periphery and were usually gathered around a small blood vessel or capillary. Many nodules, however, exhibited no blood vessels whatever. While especially numerous in the gray substance, they were also found in other areas, as the stratum zonale of the cortex, the molecular layer of the cerebellum and the optic chiasm.

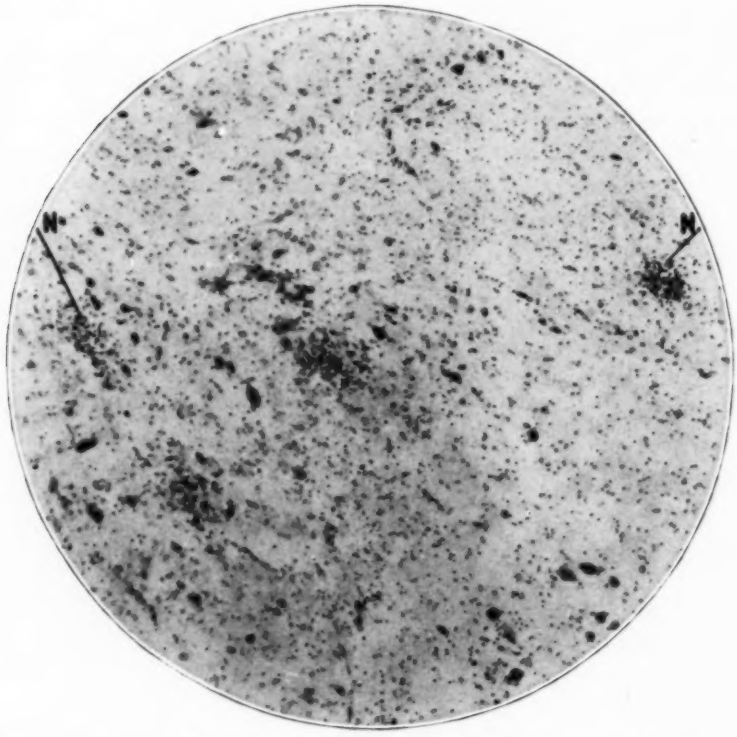

Fig. 1.—Upper cervical region. A group of nodules scattered among well preserved ganglion cells. The cell bodies making up the nodules are reproduced under a higher magnification in Figure 2. Toluidin blue × 70.

In size the nodules were sometimes quite small, especially in the cortex; in the basal ganglia, and particularly in the medulla, they were larger and also more numerous. The smaller foci, however, might be considered, as Spielmeyer [4] suggested, as fragments of a larger nodule cut off from the "poles" in the process of sectioning.

4. Spielmeyer, W.: Die zentralen Veränderungen beim Fleckfieber und ihre Bedeutung für die Histopathologie der Hirnrinde, Ztschr. f. d. ges. Neurol. u. Psychiat. (Orig.) **47**:1, 1919.

Ganglion cells were exceedingly rare inside the nodules, but around them they occurred in the usual numbers and were more or less well preserved. Hemorrhages, lipoid substances and inflammatory vascular phenomena were absent entirely. The sole makeup of the nodules were nuclei with an appreciable amount of cytoplasm. Sometimes the cytoplasmic processes of several neighboring cells merged to form a syncitium, appearing as a uniform, homogeneous mass covered with numerous nuclei (Fig. 3). In other instances the syncitial substance was more or less rarefied, or liquified, as it were, the cell bodies appearing loosely scattered.

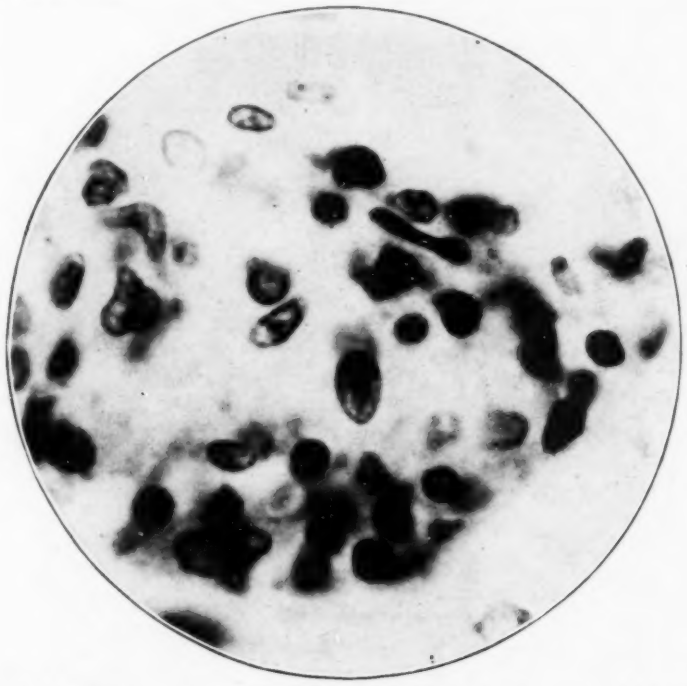

Fig. 2.—Multiform cells of a nodule; described in the text. Toluidin blue × 1200.

These cell bodies are looked on by the majority of histologists as glial elements, but by some (Piette [5]), as polyblasts. The former interpretation is more likely correct, for they were found in areas in which the blood vessels showed no changes whatever; in addition, they resembled the distinct glia cells of similar foci in lethargic encephalitis and epidemic poliomyelitis. In some regions (for example the corpora quadrigemina and around the Sylvian aqueduct) the glial

5. Piette, E. K.: Pathologic Morphology of the Brain in Typhus Fever, Vrachebnoye Dielo, No. 12-15, 1920 (in Russian).

nature of the nodules could be well demonstrated, while in other areas (the cortex) there were also present, especially on the periphery, hematogenous elements, such as lymphocytes and plasma cells (Fig. 4), while polymorphonuclear elements, glia and nerve fibers were absent.

Glia Changes.—These were mainly represented by the nodules already described. Glial proliferative phenomena in the form of satellitosis were seen only in the optic chiasm where they showed as rings or walls around small vessels. The interesting glia changes

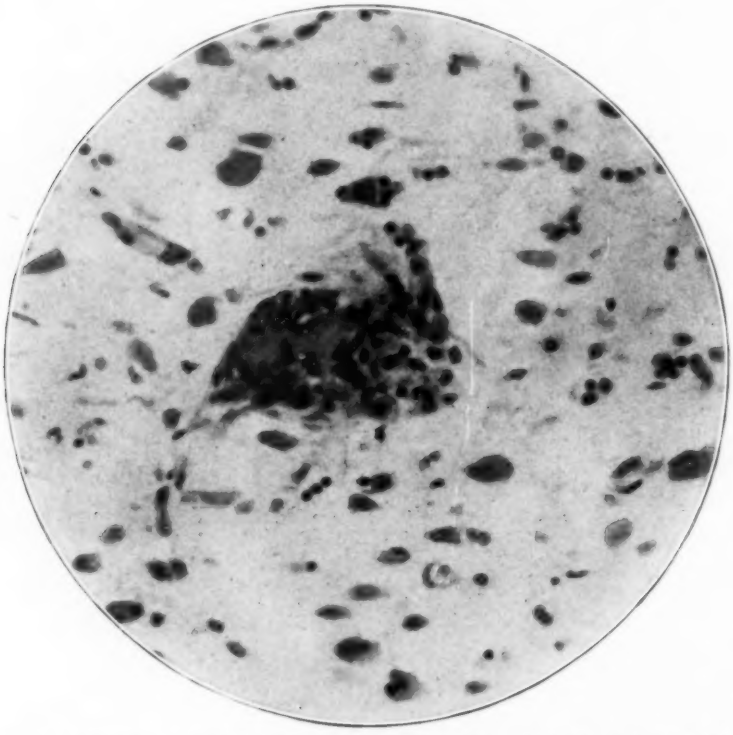

Fig. 3.—Cortex. A nodule of syncitial glial cells. Toluidin blue × 300.

described by Spielmeyer [4, 6] as bush-like ("Strauchwerk") proliferation in which proliferated glia cells form syncitial bands investing the cell bodies or their processes were not present in my cases.

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6. Spielmeyer, W.: Ueber die Hirnveränderungen beim Fleckfieber, Ztschr. f. d. ges. Neurol. u. Psychiat. (Ref.) **17**:271, 1919; Die Kleinhirnveränderungen beim Typhus in ihrer Bedeutung für die Pathologie der Hirnrinde, München. med. Wchnschr. **66**:313 and 709, 1919; Ueber einige Beziehungen zwischen Ganglienzellveränderungen und gliösen Erscheinungen, besonders am Kleinhirn, Ztschr. f. d. ges. Neurol. u. Psychiat. **54**:1, 1920.

Equally rare were the cytoplasmic glia cells, in contrast to rod-cells which were very common (Fig. 4). A remarkable feature was the association of glia cells with plasma cells which were freely scattered through the parenchyma even far away from the blood vessels (Fig. 4).

Often the glia cells showed minute dust-like lipoid granules, but myeloclasts, myelophages, gitter cells and other progressive phenomena were absent. Regressive changes in the glia, such as ameboid transformation, were also absent. Rarefication of glia, so-called reticular glia, was very marked in the cortex.

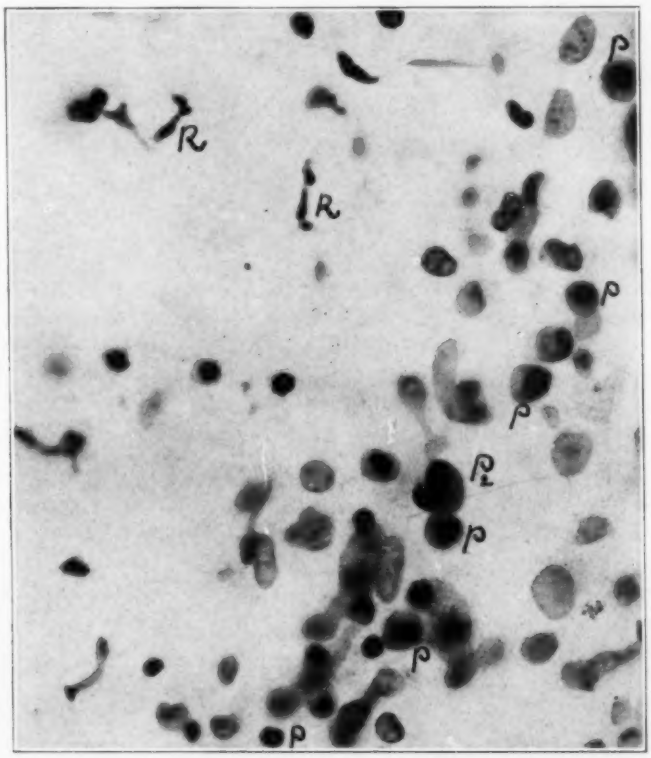

Fig. 4.—Cellular invasion of the cortex; *P.P.P.*—plasma cells; at P^2—a plasma cell with two nuclei; *R.R.*—rod cells; the dark homogeneous nuclei are lymphocytes; the pale large nuclei are glia cells; the pale eccentric curved nuclei are polyblasts; no blood vessels nor polymorphonuclear cells. Toluidin blue $\times 750$.

The diffuse glia changes were thus insignificant, as compared with the focal changes that resulted in the formation of nodules.

Ganglion Cell and Nerve Fiber Changes.—The ganglion cells exhibited changes in the cortex, basal ganglia, cerebellum, medulla and elsewhere. The intensity of the changes varied from slightly swollen cells to complete homogenization, disintegration and dissolution. The

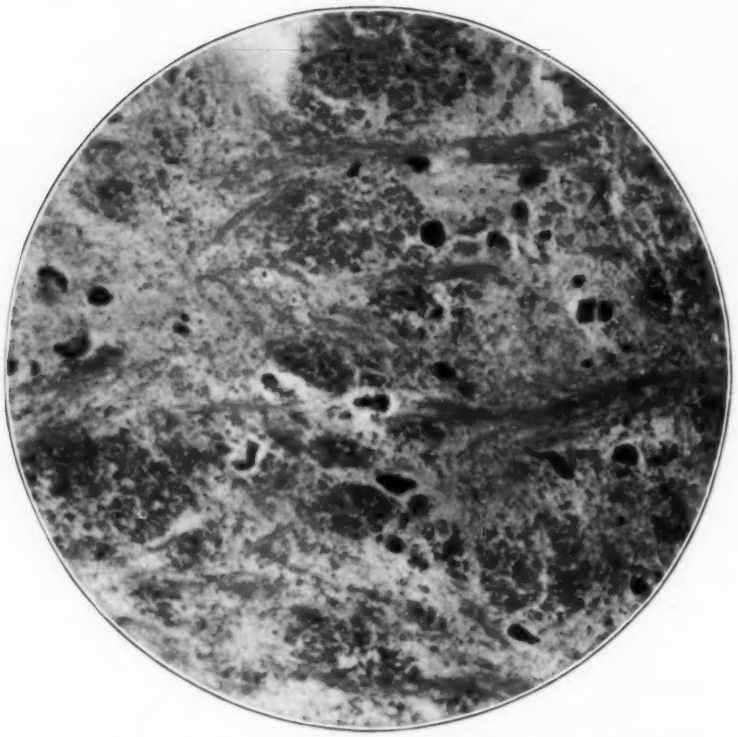

Fig. 5.—Medulla oblongata: The ganglion cells are packed with lipoids. Scarlet red-hematoxylin × 170.

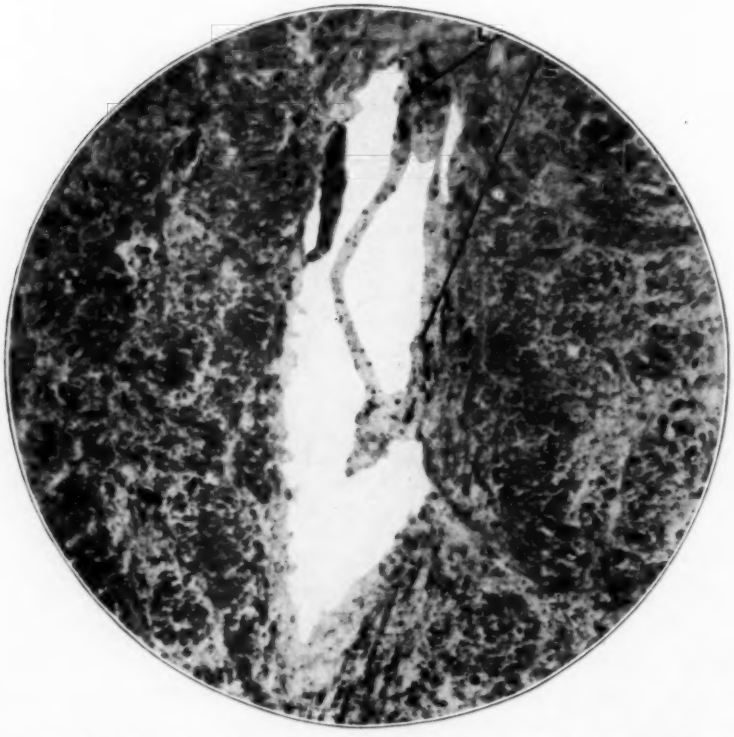

Fig. 6.—Lipoids (*L*) in the wall of a blood vessel and in the ganglion cells. Stain and magnification as in Figure 5.

nuclei were usually pale, frequently filled with granules (karyorrhexis), and the membrane was folded. Stained according to Bielschowsky's method or with toluidin blue and similar stains, they showed distinct vacuoles, appearing lattice-like. When stained with scarlet red they were found to be densely packed with lipoids (Fig. 5). These lipoids in many instances, not only filled the cell body, obscuring the nucleus, but even invaded the processes.

The fibrillary structure was retained, the fibrils sometimes appearing agglutinated and pushed toward the periphery. Neither satellitosis nor neuronophagia was common. Ganglion cells within the nodules or in their immediate neighborhood were especially damaged. Here they appeared as fragments or mere shadows.

Blood Vessels.—These always exhibited changes: hyperemia, thrombi, prominence of endothelial and adventitial cell bodies, and infiltration of Virchow-Robin spaces. Especially striking was the infiltration of the minutest capillaries with plasma cells. These cells by far predominated, often contained two nuclei and frequently invaded the parenchyma (Fig. 4) where, as pointed out, they were found in company with glia cells. Besides plasma cells there were also present lymphocytes and polyblasts, but no polymorphonuclear cells. In general, the perivascular infiltrations were in the form of thin rings.

The vessels within the nodules exhibited no infiltrations, but their endothelium appeared swollen and prominent. The endothelial cells were also prominent in capillaries that were devoid of infiltrations. Here also the adventitial cells were swollen, appeared proliferated, and in the majority of cases contained lipoid substances (Fig. 6). Proliferation and desquamation of endothelial elements, and necrosis of the vessel walls were absent. The vascular changes noted were very general, but much less marked (especially the perivascular infiltrations) in the substantia nigra and the peduncles.

Choroid Plexus.—The tuft cells of the choroid plexus (of both the lateral and fourth ventricles) were swollen and granular; often they were vacuolated or homogeneous and liquefied. Their nuclei were pyknotic and for the most part misplaced to the bottom of the cell; they contained numerous droplets of chromatin and appeared as if broken up. In some instances the tuft cells were scattered singly, mixed with plasma cells, which were exceedingly numerous, investing the blood vessels. Stained with scarlet red, the stroma of the choroid plexus showed an enormous amount of lipoids (Fig. 7), in the form of drops, droplets or minute granules. Very few lipoid granules were found within the tuft cells themselves, but they were abundant in the ependymal cells which were markedly proliferated (Fig. 8). A noteworthy feature was also an unusual number of corpora arenacea in the choroid plexus of the lateral ventricles (Fig. 9).

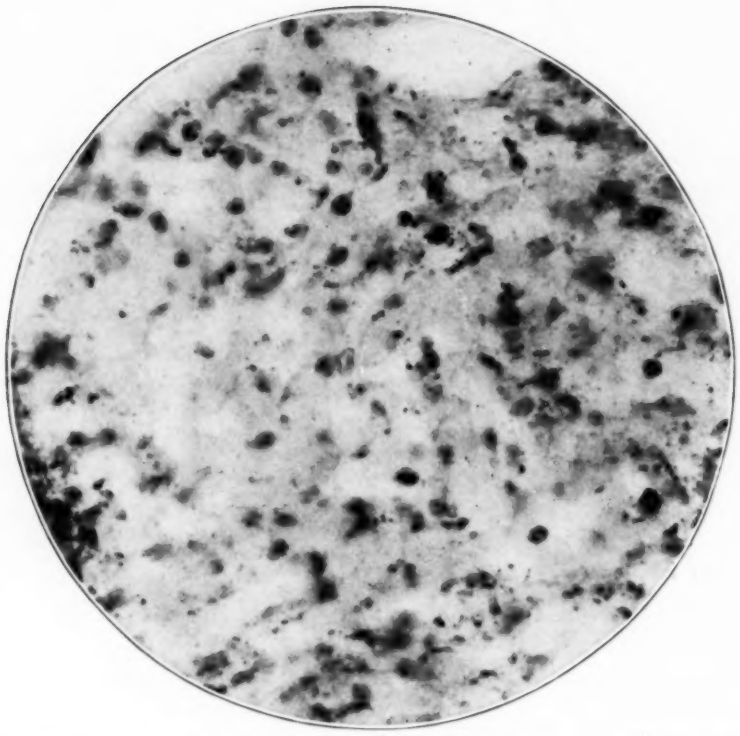

Fig. 7.—Lipoids in the stroma of the choroid plexus. The tuft cells are pale and contain only a few granules of lipoids. Scarlet red-hematoxylin × 250.

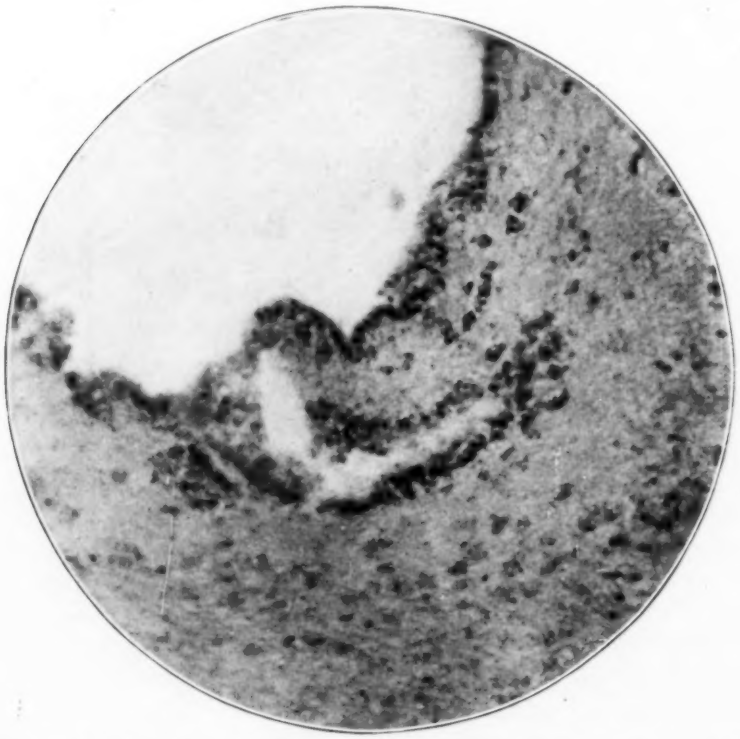

Fig. 8.—Ependymal cells of the fourth ventricle, packed with lipoids and proliferated. Stain and magnification as in Figure 5.

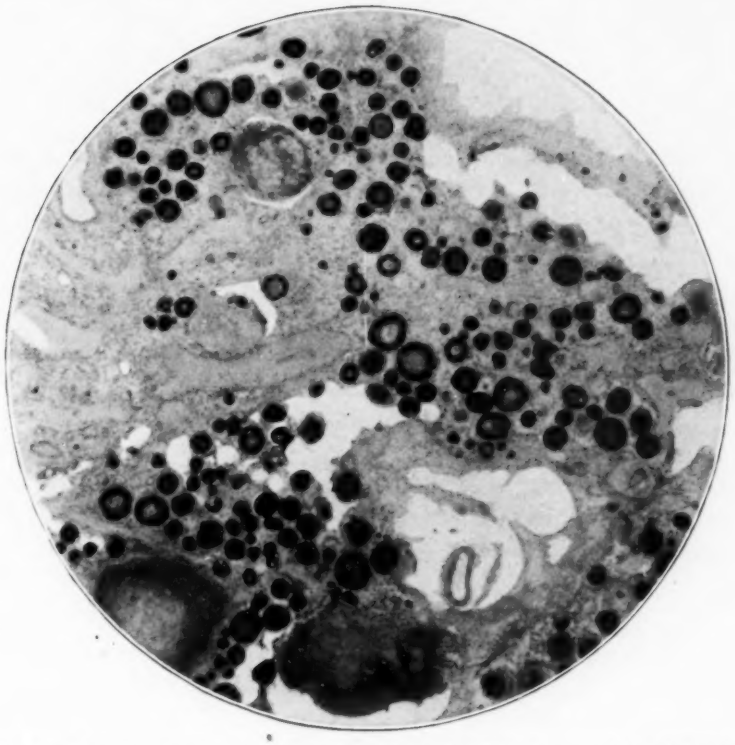

Fig. 9.—Masses of corpora arenacea in the choroid plexus of the lateral ventricles. Hematoxylin eosin × 40.

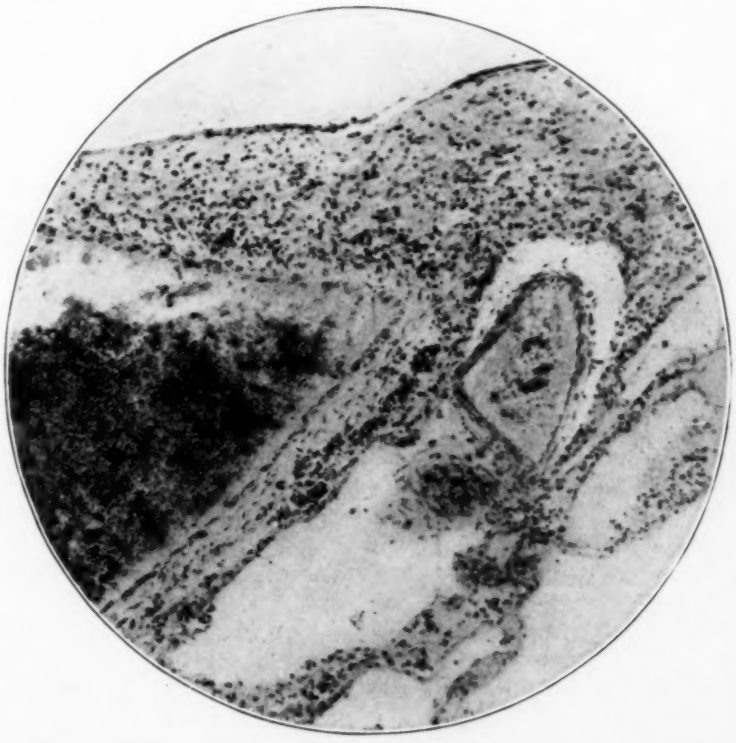

Fig. 10.—Infiltration of the subarachnoid space. Some of the infiltrating cells are reproduced in Figures 11 and 12. Toluidin blue × 70.

Meninges.—These showed universal changes—over convolutions as well as over the sulci and the spinal cord. The arachnoid exhibited large masses of mesothelial cells while the pia contained a great variety of cell bodies (Fig. 10): lymphocytes, polyblasts and plasma cells. Some of the pial elements appeared vacuolated with an eccentric nucleus and somewhat resembled macrophages (Fig. 11). These were especially in evidence over the occipital lobe where they showed inclusions (pigment). Over the sulci, infiltration of the pia-arachnoid was more marked than over the convolutions, the frontal lobe being more involved than any other portion of the brain. In addition, there were large numbers of amyloid bodies in the subpial portions adjacent to the brain tissues, and numerous gitter cells packed with lipoids were scattered throughout the entire subarachnoid space (Fig. 12).

GENERAL SUMMARY

The changes observed may be summed up as inflammatory and degenerative. The former consisted of vascular infiltrations, especially of the capillaries, combined with invasion of the parenchyma by plasma cells. The degenerative phenomena showed as infiltration of the ganglion cells with lipoids, associated with mild diffuse and marked focal glial profileration (nodule formation). In addition there was invasion of the meninges and the choroid plexus with hematogenous elements and lipoid substances.

CONTRAST BETWEEN THE TYPHUS BRAIN CHANGES AND THOSE OF EPIDEMIC ENCEPHALITIS AND EPIDEMIC POLIOMYELITIS

The nodules found so abundantly in typhus fever not only in the brain, but also in the skin, heart, kidneys and other organs, were correctly described by Popoff [7] in 1875, and more fully by Fraenkel [8] in 1914. By some authors (Benda,[9] Dabrowsky,[10] Nicol [2]) they are considered specific for this disease. Jahrisch [11] found them in fifteen out of sixteen cases, and Davidowsky [12] missed them in only three out

7. Popoff: Ueber die Veränderungen im Gehirn bei Flecktyphus, Centrlbl. f. d. med. Wissensch. **13**:596, 1875.

8. Fraenkel, E.: Ueber Fleckfieber u. Roseola, Münch. med. Wchnschr. **61**:57, 1914; Anatomische Befunde bei Flecktyphus, Ibid. p. 1534.

9. Benda, C.: Mikroskopisch- pathologische Befunde im Gehirn eines Fleckfieberfalles, Ztschr. f. ärztl. Fortbld. **12**:464, 1915.

10. Grzywo-Dabrowski, W.: Untersuchungen über die pathologische Anatomie des Fleckfiebers, Virchow's Arch. f. path. Anat. **225**:299, 1918.

11. Jahrisch, A.: Zur Kenntniss der Gehirnveränderungen bei Fleckfieber, Deutsch. Arch. f. klin. Med. **126**:270, 1918.

12. Davidowsky, I.: Pathologic Anatomy and Pathology of Typhus Fever. Vol. 1, 1920, Moscow (in Russian).

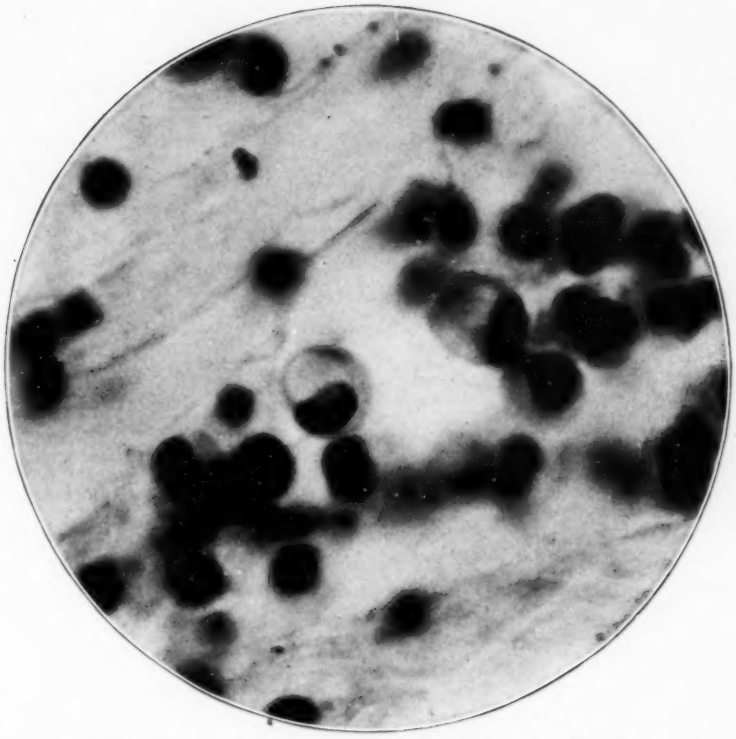

Fig. 11.—Some of the infiltrating elements in Figure 10. The large vacuolated cell bodies with an eccentric nucleus are macrophages.

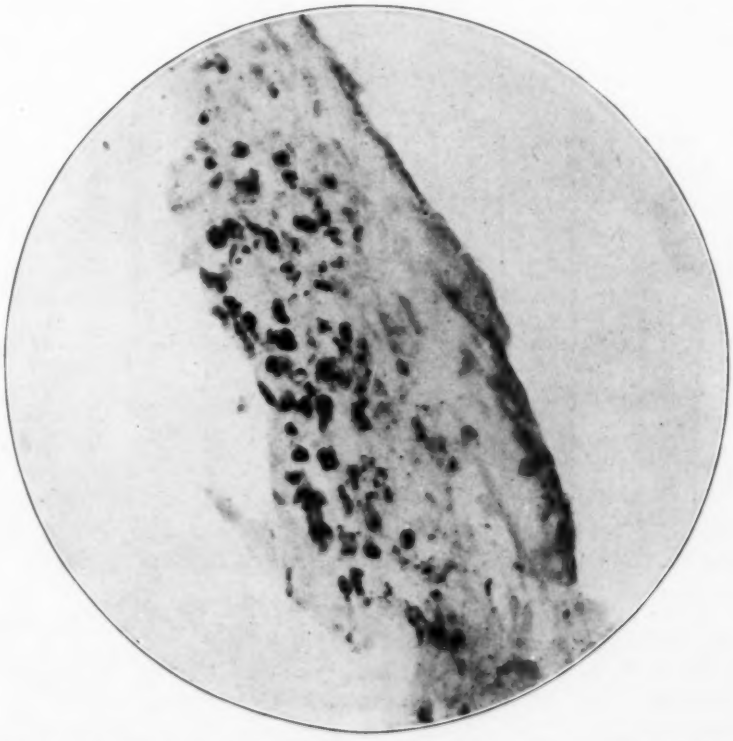

Fig. 12.—Lipoids enclosed with gitter cells. Surface section of the pia. Scarlet red × 13.

of seventy cases. However, nodules are also present in other diseases, such as typhoid fever and, as the appended photomicrographs (Figs. 13 and 14) show, also in epidemic encephalitis and poliomyelitis. In epidemic encephalitis they predominate in the midbrain and basal ganglia and may be found also in the spinal cord, but not in the cerebral cortex or cerebellum—the common sites of nodules in typhus fever. In poliomyelitis they are quite common in the ventral horns of the spinal cord and in the so-called cerebral forms of this disease they are present in the pons and region of the Sylvian aqueduct, but, again, not in the cerebrum or cerebellum. Thus, the specific feature is not their presence in typhus fever, but their abundance and widespread dissemination which spares no part of the nervous system, though it is claimed by the majority of observers that the medulla oblongata is the principal portion involved.

Equally non-specific are the diffuse glia changes. They are in varying degrees present in all these three diseases, in the form of cytoplasmic glia, that is to say, as mild proliferative or progressive phenomena. However, in some cases of poliomyelitis, regressive glia changes may be seen in the form of ameboid glia cells (Walter,[13] Hassin [14]) which have not been described in epidemic encephalitis and especially not in typhus. As compared with focal proliferation of the glia resulting in nodule formation, diffuse glial proliferation, in all the three diseases, is rather mild. While more or less in evidence in poliomyelitis, especially in the ventral horns of the spinal cord, it is less so in epidemic encephalitis, and still less in typhus. In short, the reactive glia phenomena in poliomyelitis, epidemic encephalitis and typhus fever, though fundamentally alike, differ in intensity, extent and probably also in location. Such differences are most likely due to the dissimilar nature of the virus. In each of the three conditions the virus provokes a different reaction of the glia tissue.

As to the ganglion cells, in both typhus and epidemic encephalitis these exhibited rather mild changes, while in polyomyelitis they are as a rule severe (marked satellitosis, neuronophagia and total cell dissolution). They may also be very marked in typhus fever, especially in the areas occupied by nodules, so that we might maintain, as to the type and the character of the ganglionic changes, that typhus fever combines the features of both epidemic encephalitis and anterior poliomyelitis. Yet the changes are not specific, merely being, like the nodular formations, more widespread and showing more abundant lipoid accumulation than in either of the other two diseases.

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13. Walter, R.: Zur Histopathologie der akuten Poliomyelitis, Deutsch. Ztschr. f. Nervenh. **45**:79, 1912.

14. Hassin, G. B.: A Contribution to the Histopathology of Human and Experimental Poliomyelitis, Med. Rec. **92**:89 (July 21) 1917.

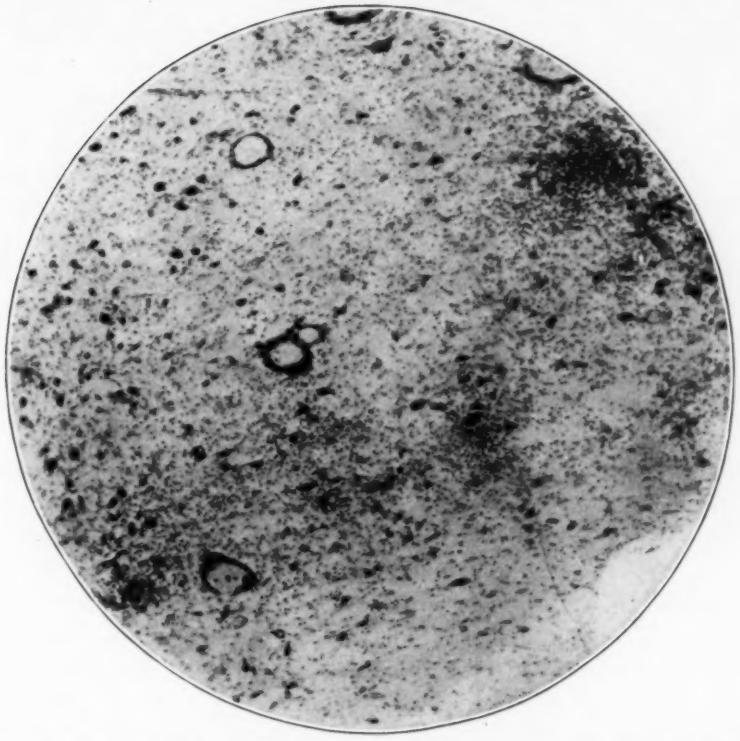

Fig. 13.—Case of poliomyelitis: Locus coeruleus—dense foci or nodules and numerous infiltrated blood vessels. Compare with Figures 1 and 14. Toluidin blue ×60.

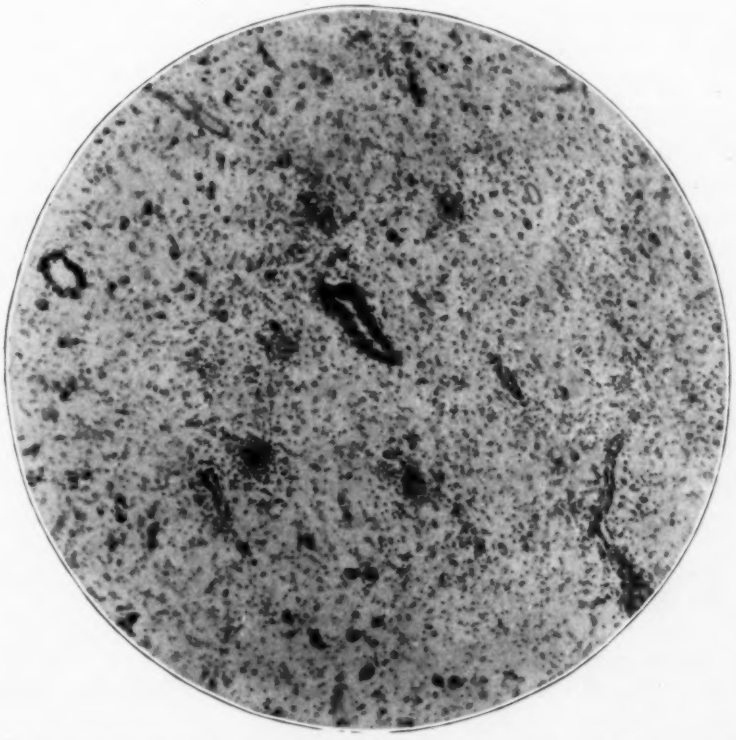

Fig. 14.—Case of epidemic encephalitis: Region of the Sylvian aqueduct—nodules and infiltrated blood vessels. Compare with Figures 1 and 13. Toluidin blue ×60.

Significant as the ectodermal (glia and ganglionic) changes are in all three diseases, the mesodermal changes are even more striking. They are mainly represented by the condition of the blood vessels. In typhus fever this has attracted particular attention, some authors (Bauer [15]) defining typhus as a "disease of the smaller vessels." The very origin of the nodules was ascribed by many pathologists (Jahrisch,[11] Herzog,[16] Bauer,[15] Ceelen,[3] Gross [17]) to necrosis of the endothelium of the blood vessels which they thought was the primary phenomenon — the essential factor — the brain changes being secondary to the vascular destruction. The vascular change they thought was brought on by the virus, which caused proliferation of endothelium, it degeneration, desquamation and necrosis. The vascular changes were therefore characterized as desquamative endarteritis (Herzog, Ceelen, Bauer) or thrombovasculitis (Davidowsky). However, comparative studies of nodule formation, as well as of ectodermogenic changes, in both epidemic encephalitis and poliomyelitis, show that neither have anything to do with the blood vessels, all the changes—vascular, glial and ganglionic—being directly due to the virus. Necrosis of the blood vessels, to which is ascribed the formation of the nodules, has not been found in either epidemic encephalitis or poliomyelitis though nodules in the brain may be as numerous in them as in typhus fever. But even in typhus, vascular necrosis is denied by so competent a neuropathologist as Spielmeyer. On the other hand, the vascular system does exhibit in this disease, as in epidemic encephalitis and poliomyelitis, marked progressive and active phenomena. These show as perivascular, or more correctly, adventitial infiltrations of the smallest capillaries with lymphocytes and especially with plasma cells, marked hypertrophy of the endothelial cells and hyperplasia of the adventitial cells. In both poliomyelitis and epidemic encephalitis the larger blood vessels are principally, but not exclusively, infiltrated. In the former this obtains mainly in the gray and white substances of the spinal cord; in epidemic encephalitis chiefly in the midbrain and basal ganglia. Here the infiltrations show as dense rings or "muffs" which in typhus are very uncommon, the smallest capillaries, as pointed out, being principally involved. The infiltrations in typhus fever are therefore less striking and less evident, but they affect much larger areas. Like the ectodermal

15. Bauer, E.: Zur Anatomie und Histologie des Flecktyphus, Münch. med. Wchnschr. **63**:541 and 1243, 1916.

16. Herzog, G.: Zur Pathologie des Fleckfiebers, Centralbl. f. allg. Path. u. path. Anat. **29**:97, 1918.

17. Gross, W.: Ueber Encephalitis, Virchow's Arch. f. path. Anat. **242**:452, 1923.

(glial, ganglionic) changes they are more diffuse and more widespread, covering not only the entire central nervous system, but according to Davidowsky, also the sympathetic system and peripheral nerves.

Also more severe in typhus are the changes in the choroid plexus and the pia-arachnoid. So great a wealth of cellular elements and lipoids as is exhibited by these formations in typhus fever, is not seen either in poliomyelitis or epidemic encephalitis.

COMMENTS

Central nervous system changes in typhus fever are those of an acute nonsuppurative encephalomyelitis. In their fundamental features they much resemble those found in epidemic encephalitis and poliomyelitis. The difference lies in the extent of the inflammatory and the degenerative phenomena, which in typhus are more widespread, more abundant and more pronounced than in the two other conditions. Both the inflammatory and the degenerative phenomena are to be considered as the result of the action of a specific virus which affects equally the ectodermogenic (ganglion and glia cells) and mesodermogenic (blood vessels, choroid plexus) tissues. The ganglion cells respond by degeneration and sometimes by cell dissolution; the glia by marked focal (nodular) and mild diffuse proliferation. The proliferative glia cell as well as the degenerative ganglion cell phenomena may vary in intensity and extent, depending on the individual resistance or vitality of the ganglion or glia cell bodies. However mild they are, the changes differ in this type of encephalitis from those of other forms by being decidedly more diffuse; they spare no part of the nervous system and cause therefore wider involvement of nervous tissue than occurs in encephalitis of the epidemic or poliomyelitic type. This fact probably accounts for the remarkable changes in the pia-arachnoid and the choroid plexus which is evidenced by vast accumulations of lipoid substances and various cellular elements in these structures. It is rather suggestive that the lipoids found in such large amounts in the ganglion cells of the brain, while being carried to the subarachnoid space and the lateral ventricles by way of the Virchow-Robin spaces, are partly deposited in the ependymal cells, which therefore appeared to be packed with them (Fig. 6). In addition, as pointed out in a previous contribution,[18] various toxins when discharged like the lipoids into the subarachnoid space provoke there marked cellular activity that results in proliferation of mesothelial cells, accumulation of lymphocytes, changes in the choroid plexus with abundant formation of sand bodies, etc.

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18. Hassin, G. B.: A Note on the Comparative Histopathology of Acute Anterior Poliomyelitis and Epidemic Encephalitis, Arch. Neurol. & Psychiat. **11**:28 (Jan.) 1924.

CONCLUSIONS

1. The changes in the central nervous system in typhus fever are those of an acute disseminated encephalomyelitis, nonsuppurative in character.

2. It much resembles other forms of encephalitis, such as the epidemic type and that occurring in some forms of poliomyelitis.

3. It differs from the two types mentioned by the wider distribution, by lack of preference for certain areas and by the presence of more pronounced degenerative changes.

4. The subarachnoid and choroid plexus changes are also considerably more marked, which is probably in accordance with more severe and more widespread parenchymatous changes.

5. The nodules are by no means typical of typhus, for they occur also in epidemic and poliomyelitic types of encephalitis.

6. The nodule formation is not due to vascular disorder, but is the result of the action of a specific virus.

7. In typhus fever the virus is responsible for both the inflammatory and the degenerative changes in the central nervous system.

CONCERNING THE CEREBELLAR SYMPTOMS PRODUCED BY SUPRASELLAR TUMORS*

PERCIVAL BAILEY, M.D., PH.D.

BOSTON

That neoplasms of the brain may give rise to disorder of parts of that organ far distant from the actual site of the growth, due to distortion, edema, pressure, internal hydrocephalus, or other reasons, is well known. To such an extent is this true that it may be difficult to determine even whether the tumor lies above or below the tentorium. Thus, certain signs and symptoms generally associated with lesions of the cerebellum may be produced by destructive injuries of the cerebrum. Bruns [1] long ago called attention to ataxia with tumors of the frontal lobes in the absence of disturbance of voluntary motion, of muscular sense or of the reflexes. A certain amount of passivity also may be found in these cases. Injuries to the parietal lobe may cause some dysmetria, asynergia, and passivity in the extremities of the opposite side of the body; they may even cause past pointing according to Rothmann.[2] Trauma of the temporal lobe may give rise to similar difficulties. The pendular reflex is present in some cases of lesion near the motor zone, with a flaccid hypotonic hemiparesis.

Usually it is easy to determine the seat of origin of these manifestations both by the phenomena which accompany them, and also by the lack of certain other phenomena which would be present if the lesion were in the cerebellum. Claude Vincent [3] has pointed out that ataxia due to injury of the frontal lobe is not attended by adiadokokinesis, asynergia, dysarthria or hypermetria. The dysmetria, asynergia and passivity of parietal lobe origin are usually distinguished by the intensity of the sensory phenomena which accompany them. The flaccidity of certain hemiplegias is due to relaxation of the ligaments and not to the state of resistance of the muscles. One finds also a diminution in the speed of muscular action instead of the abruptness of movement seen with lesions of the cerebellum. Usually also the paresis is too great to be explained by the slight diminution in force caused by destruction of the cerebellum.

It is not the phenomena just described, then, which give rise to error, but rather the disturbances of equilibration. Equilibratory

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*From the Surgical Clinic of Dr. Harvey Cushing, Peter Bent Brigham Hospital, Boston.

1. Bruns: Deutsch. med. Wchnschr. **18**:138, 1892.
2. Rothmann: Neurol. Centralbl. **33**:3, 1914.
3. Vincent: Rev. neurol. **21**:209, 1911.

troubles are of the greatest importance in diagnosing lesions of the cerebellum in the absence of sensory disturbances of the lower extremities, of general physical weakness, and when the vestibular apparatus is intact. Stupor and high intracranial tension are two other factors which make the interpretation of disequilibration difficult.

Many patients have high intracranial tension, stupor, and, if they get on their feet, show a tendency to fall backward. Moreover they are apt to be so uncooperative because of stupor and pain that neurologic study is difficult. Such a patient may have a tumor either in one of the so-called silent areas of the cerebrum (frontal, parieto-occipital, or temporal) or in the middle of the cerebellum. In these cases great weight must be given to a careful history, with especial attention to the chronological order of appearance of the symptoms. Disequilibration is apt to occur early with tumors of the cerebellum because it is due to local injury; it occurs late with supratentorial tumors because it is due to increased intracranial tension.

But it is not only new growths in the silent areas of the cerebrum which may be confused with tumors of the cerebellum. It has been known for a long time that neoplasms in the cerebellum as well as in other parts of the intracranial cavity may cause symptoms of pituitary disorder (adiposity, genital dystrophy, destruction of the sella turcica, etc.) due to the dilatation of the third ventricle by the resulting internal hydrocephalus.[4,5] A good history usually suffices to determine that the pituitary manifestations are secondary. It is less common for the reverse to occur; namely, for a tumor of the pituitary region to give rise to symptoms suggestive of cerebellar disorder. For this reason the following cases are recorded.

REPORT OF CASES

CASE 1.—10563.—*Suprasellar tumor with cerebellar symptoms. Decompression. Cerebellar exploration. Trans-sinus puncture. Transfrontal exploration. Necropsy.*

J. P., an Italian schoolboy, aged 14, was admitted June 1, 1919, complaining of headaches, convulsions and failing vision, having been referred by Dr. J. W. Courtney of Boston. Four years previously the patient complained of stiffness of the back of his neck and double vision for a short period. One year before admission he developed severe right internal strabismus and was told that he had a brain tumor. During the last year his vision had failed, with periods of increased amblyopia. The last two months he had been unable to read and had had occipital headaches accompanied by vomiting. In the last three weeks he had had several severe generalized convulsions, and had developed marked difficulty of speech.

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4. Cushing: J. Nerv. & Ment. Dis. **44**:415 (Nov.) 1916.
5. Strauch: J. A. M. A. **72**:1731 (June 14) 1919.

Examination.—On admission he was apathetic and unresponsive. There was a cracked-pot note on percussion of the head, pressure exophthalmos, and dilatation of the veins around the eyes. The pupils were dilated and reacted very sluggishly to light. The patient was practically blind, with bilateral choked disk of 4 to 5 diopters. There were: left facial weakness, dysarthria, reeling gait with tendency to deviate to the right, *chute en arrière*, marked general hypotonicity of the musculature, and considerable incoordination particularly of the left arm and leg. In bed, he kept the head hyperextended with neck rigid; he stood with exaggerated lordosis and a tendency to fall backward. There was a fine tremor of the outstretched hands. The roentgenogram showed: the anterior clinoids short and stubby; the posterior clinoids and dorsum sellae practically obliterated. No suprasellar shadow was seen. The genitalia were somewhat underdeveloped and the pubic and axillary hair were scanty.

First Operation.—June 21, 1919, Dr. Cushing performed a subtemporal decompression during which ventricular puncture demonstrated internal hydrocephalus.

Postoperative Course.—There was no improvement in the condition.

Second Operation.—July 3, 1919, Dr. Cushing made a suboccipital exploration, but no lesion was disclosed.

Postoperative Course.—The patient made rapid improvement for a week or so and then became rapidly again semicomatose.

Third Operation.—July 24, 1919. In an attempt to establish transsinoidal drainage, Dr. Cushing turned down a bone flap, exposing the longitudinal sinus. Punctures were made through the sinus into the ventricle in two places with a lumbar puncture needle, and a silver cannula was inserted, leading from the sinus presumably into the ventricle.

Postoperative Course.—The patient improved steadily and was discharged Sept. 14, 1919. At that time he was mentally alert and able to stand alone. There were tremor of the hands, stammering speech, and bilateral secondary optic atrophy with total blindness. The decompressed areas were bulging. He entered the Perkins Institute for the Blind where he did good work and learned to read braille. He was able to walk around during this time and the decompressed area in the right temporal region was flat.

In September, 1921, he became weaker, could not walk, lost appetite and had to go to bed. After a month he improved and was doing odd jobs around the house, but since January, 1922, he had been in bed suffering from headaches and occasional vomiting. The decompressed areas had been gradually filling out again.

Examination on Readmission.—July 20, 1922. At this time the subtemporal decompression area was tense and bulging. There was no elevation of the optic disks. Speech was hesitating and staccato but not dysarthric. He was euphoric and mentally alert. The knee jerks and ankle jerks were exaggerated, but there was no clonus nor Babinski's phenomenon. The gait was somewhat spastic. Nystagmus was present on looking to the right and to the left. The latter symptom was discounted because of the blindness. As on his previous admission it was noted that the genitalia were somewhat underdeveloped and that pubic and axillary hair were very scanty. The basal metabolism was —29. A new roentgenogram was taken which showed for the first time a suprasellar shadow made by calcification in a congenital cyst.

Ventriculography.—July 31, 1922. Under local anesthesia 140 c.c. of fluid were withdrawn from the right ventricle and replaced by 120 c.c. of air. Stereoscopic films showed general dilatation of the ventricular system. The third

ventricle was not definitely outlined, but air was seen at the base of the skull in the lateral film taken with the chin up, which seemed to be in the third ventricle. No tumor mass could be outlined.

Fourth Operation.—Aug. 12, 1922, Dr. Cushing turned down a right frontal bone flap without difficulty. A needle inserted through the hemisphere toward the third ventricle to a depth of 3 cm. struck fluid which contained no cholesterin crystals or other evidence of having come from a cyst. The needle was left in place. The chiasm was exposed, the anterior legs not being separated by tumor as is usually the case. It seemed somewhat flat, however, so the region behind and between the optic tracts was explored; fluid was obtained which

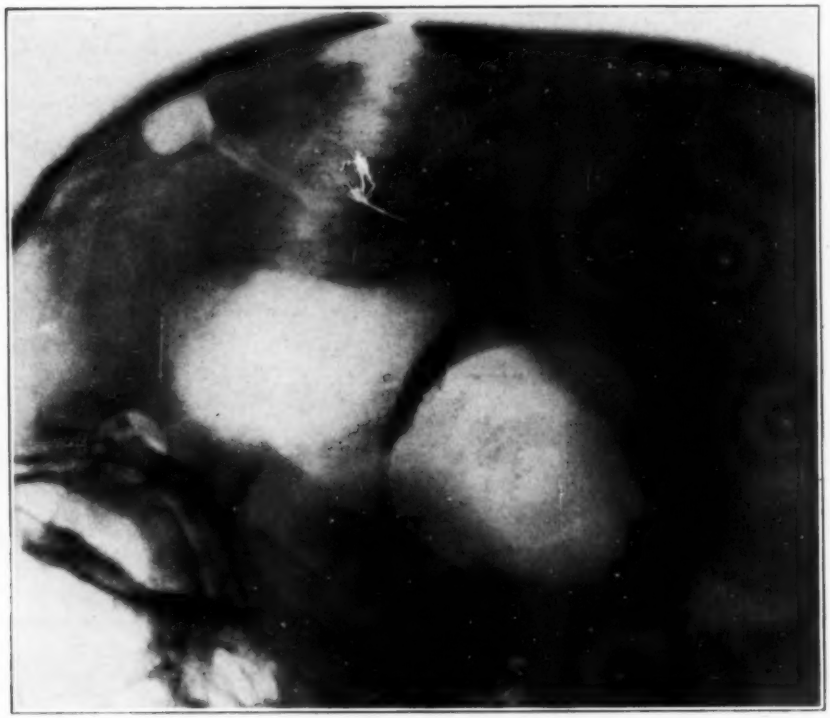

Fig. 1.—Roentgenogram taken after the cyst cavity in Case 1 had been filled with air. The shadow of the tumor is seen in the bottom of the air-filled space.

was slightly brownish and contained cholesterin crystals. Air, injected into the needle left in the hemisphere, bubbled out through the hole which had been made back of the chiasm. Since it was doubtful whether a cyst or the third ventricle had been opened, the operation was abandoned and the wound closed as usual.

Postoperative Course.—Stereoscopic roentgenograms showed a large collection of air, roughly diamond-shaped, which extended anteriorly to within 1 cm. of the surface of the cerebral cortex on the right of the midline, and posteriorly over the sella. In the bottom of this collection of air the tumor nodule could be clearly seen (Fig. 1). The patient gradually became stupid and untidy.

Ventricular punctures aroused him for a while but he soon lapsed into his former stuporous condition. Finally, on September 6, he developed marked hyperthermia and died.

Necropsy.—The brain was removed after fixation with 10 per cent. liquor formaldehydi by carotid injection. The hypophysis was somewhat flattened. The region of the third ventricle was occupied by a firm tumor mass which on sagittal section proved to be 5 by 3 cm. in size and calcified (Fig. 2). In the upper anterior part of the tumor was a large cystic space filled with greenish yellow gelatinous coagulum. The third ventricle was entirely filled by a cyst which projected into both foramina of Monroe and posteriorly into the aqueduct of Sylvius. The lateral ventricles were much dilated.

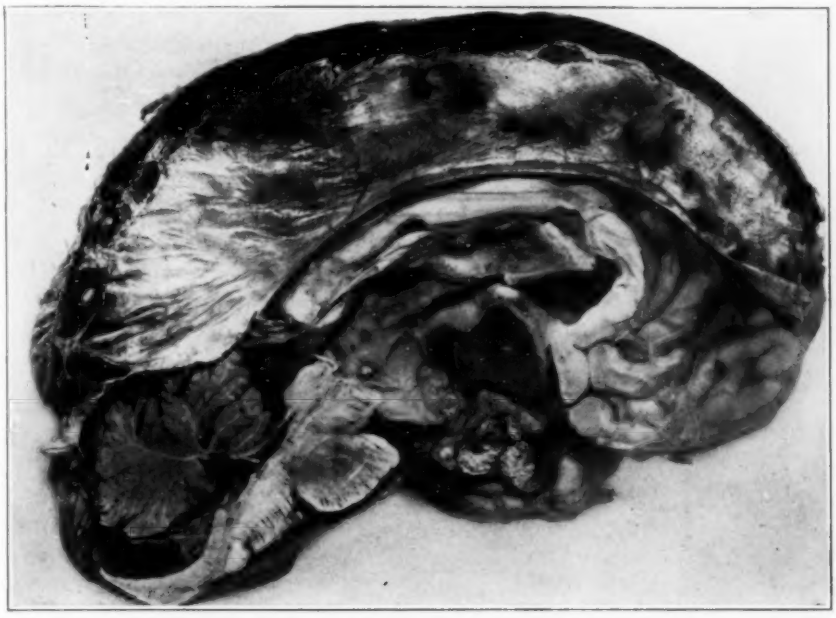

Fig. 2.—Left surface of median sagittal section of brain of J. P., Case 1.

Microscopic Examination.—This showed the tumor to be a typical suprasellar epithelioma, a tumor of Rathke's pouch, whose structure is too well known to require detailed description (Fig. 3).

Comment.—With the present perfection of radiography, this tumor would probably have been correctly localized and diagnosed at the time of the first admission, for it is to be supposed that there were calcareous deposits in the tumor at that time. The presence of a suprasellar shadow in the roentgenogram is an invaluable aid in the diagnosis.

There were many features of the clinical picture which made the diagnosis difficult. Examination of the visual fields was impossible because of blindness. Choked disk is rare with tumors in the pituitary region. Today a high degree of choked disk, with complete absence of any suprasellar shadow in the roentgenogram, is almost invariably sufficient to decide in any doubtful case

in favor of the cerebellum as the seat of the lesion. It was doubtless the combination of a high degree of choked disk and failure to demonstrate suprasellar calcification that led to an erroneous localization in the case of this boy.

CASE 2.—15381.—*Suprasellar epitheliomatous cyst with cerebellar symptoms. Transfrontal exploration. Death from hyperthermia. Necropsy.*

D. H., a child aged 6 years, was admitted Oct. 13, 1921, complaining of loss of vision, having been referred by Dr. J. W. Hammond, of Boston. "For a long time" the patient had had attacks of headache, usually frontal, that were relieved by vomiting or defecation. Just when they began is not certain, but about three years before admission severe seizures started accompanied

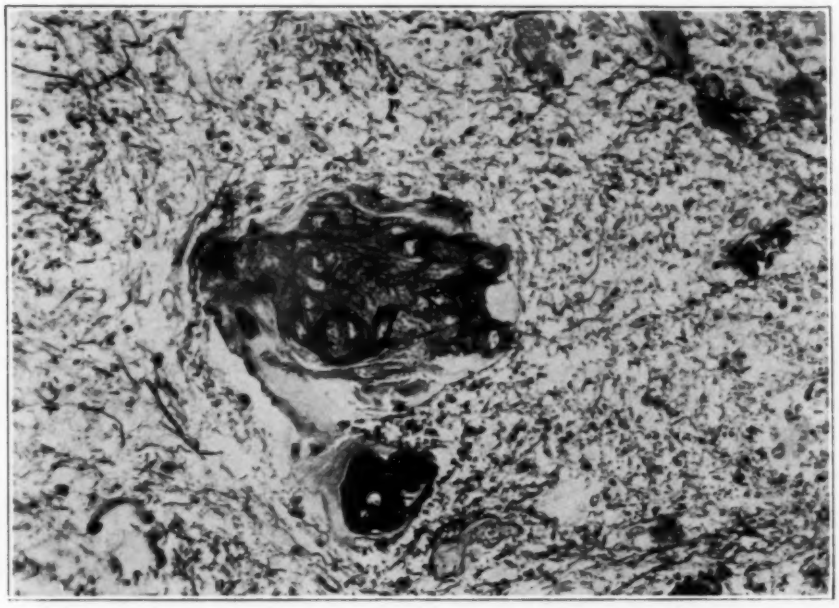

Fig. 3.—Photomicrograph of section of tumor from case of J. P., Case 1. A calcified nodule, a few cornified epithelial cells, and numerous epithelial fibrils may be seen. Neutral ethyl violet-orange G stain. × 850.

by frontal and occipital headaches and vomiting. For the last year these symptoms had ceased. During an acute exacerbation in July, 1920, she was admitted to the Children's Hospital. While there she was seen to have three generalized convulsions. At that time it was noted that she was very drowsy. The optic disks were pale and their margins were blurred. Ten months previous to admission to the Peter Bent Brigham Hospital, vision began to fail in the left eye and the loss of vision had been progressing steadily.

Examination.—Mentally she was alert. The optic disks were pale; the nasal margins were obscured, and the veins were full and tortuous. No record was made (because of poor cooperation of the patient) of the visual fields. Roentgenograms showed that the suture lines of the skull were separated; the sella turcica wa ssomewhat depressed; no suprasellar shadow was seen.

Course.—Oct. 21, 1921, the patient was discharged with a diagnosis of "suprasellar tumor; unverified." The diagnosis was not considered sufficiently certain to justify operation.

July 17, 1922, the child was readmitted. She had done well until June, when her mother noticed that she stumbled and fell while walking around the room; she had difficulty in looking down, was drowsy, and complained of headache.

Examination.—There was a cracked-pot sound to percussion over the skull. The optic disks were pale, the disk margins were blurred, and the vessels were full and tortuous. There were slight incoordination of the upper, marked incoordination of the lower extremities (hypermetria, asynergia), markedly

Fig. 4.—Roentgenogram of sella from case of D. H., Case 2. The shadow of the calcification is seen over the dorsum sellae.

reeling gait on a wide base, and *chute en arrière.* There was a questionable Babinski sign on the right side. All the reflexes were feeble and there was hypotonicity of all the limbs. Roentgenograms showed the sella rather large considering the age of the patient, with rather blunt clinoids. Just above the posterior clinoids was a faint irregular mass suggesting slight calcification (Fig. 4).

Operation.—July 26, 1922, Dr. Cushing turned back a frontal osteoplastic flap. The ventricle was punctured early. On elevating the frontal lobe and incising the dura, the bluish wall of a cyst was disclosed with, crossing it, a large anterior communicating artery. The artery was clamped and divided. The cyst was evacuated and a portion of the wall removed.

Postoperative Course.—The patient developed hyperthermia, 104 to 106, was restless and delirious, and died on the third day after the operation.

Necropsy.—On median section, the third ventricle was seen to be occupied by a large calcified tumor mass surmounted by a cyst (Fig. 5). One sees in the photograph that the anterior portion had been removed at the operation The most interesting feature of the growth was the extension of the cyst as a dog-eared projection down into the left cerebellopontile angle (Fig. 6). The pituitary body was slightly flattened.

Microscopic Examination.—As in the previous case, the growth proved to be a suprasellar epithelioma, or tumor of Rathke's pouch (Fig. 7).

Comment.—In a female child of this age it is difficult to estimate the intensity of hypopituitary disturbances. Moreover, the roentgenogram failed to reveal any suprasellar calcification. So that, although at the time of the first admission it was felt that a suprasellar tumor was present, a positive diagnosis

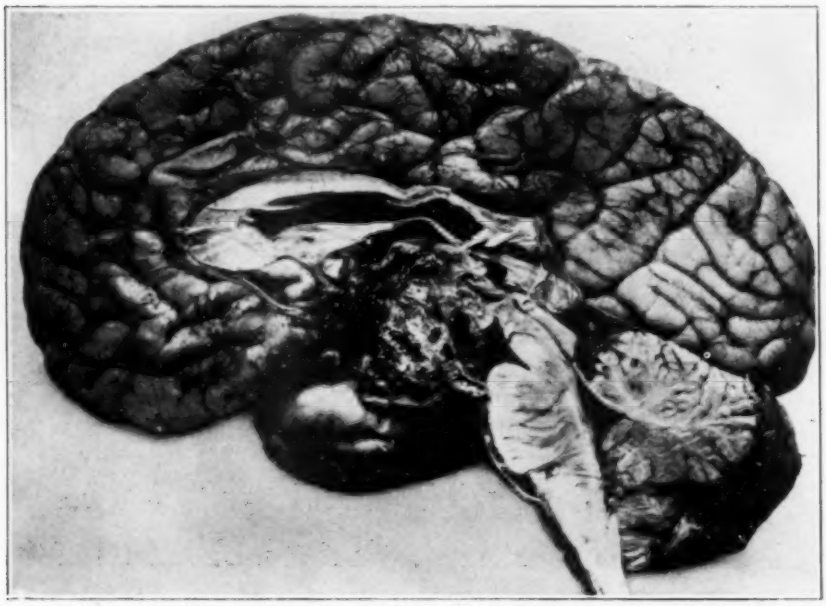

Fig. 5.—Right surface of median sagittal section of brain of D. H., Case 2.

was not made. At that time there was no question of a tumor of the cerebellum since no symptoms nor signs of a lesion of this part of the brain were present.

At the time of the second admission the clinical picture was that of a midline tumor of the cerebellum with slight secondary pituitary manifestations; confusion might easily have arisen had not the roentgenogram revealed the suprasellar calcification. In this case there was very little intracranial hypertension, and the marked hypotonicity, hypermetria, and other signs made it appear that the equilibratory disturbance was of cerebellar origin.

CASE 3.—12150.—*Suprasellar tumor with cerebellar symptoms. Decompression. Cerebellar exploration. Death at home two years later. Necropsy.*

R. M., a student, aged 17 years, was admitted March 29, 1920, complaining of headache and vomiting, having been referred by Dr. J. D. Bruce of Saginaw,

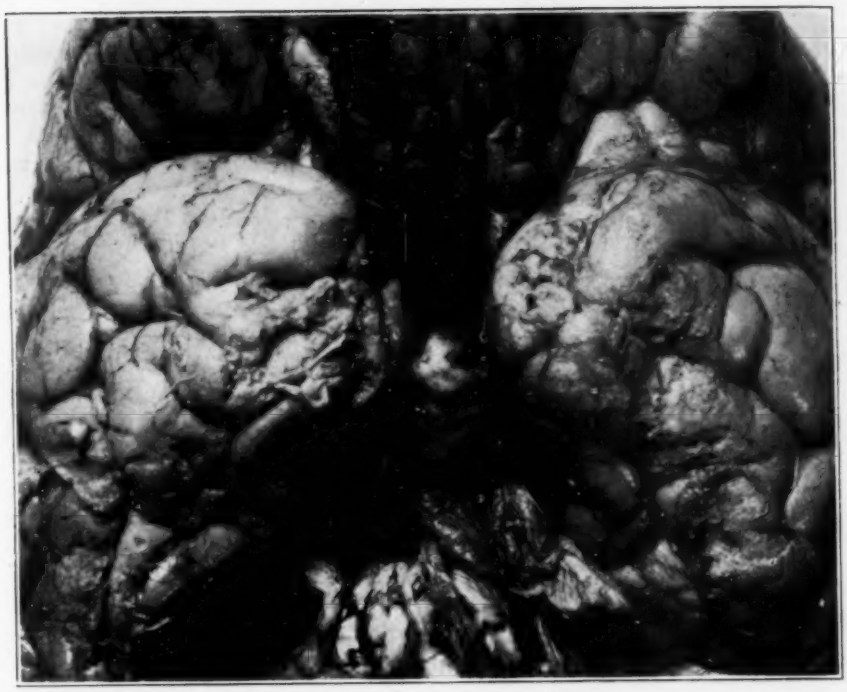

Fig. 6.—Ventral aspect of brain of D. H., Case 2. The extension of the cyst downward into the left cerebellopontile angle is seen.

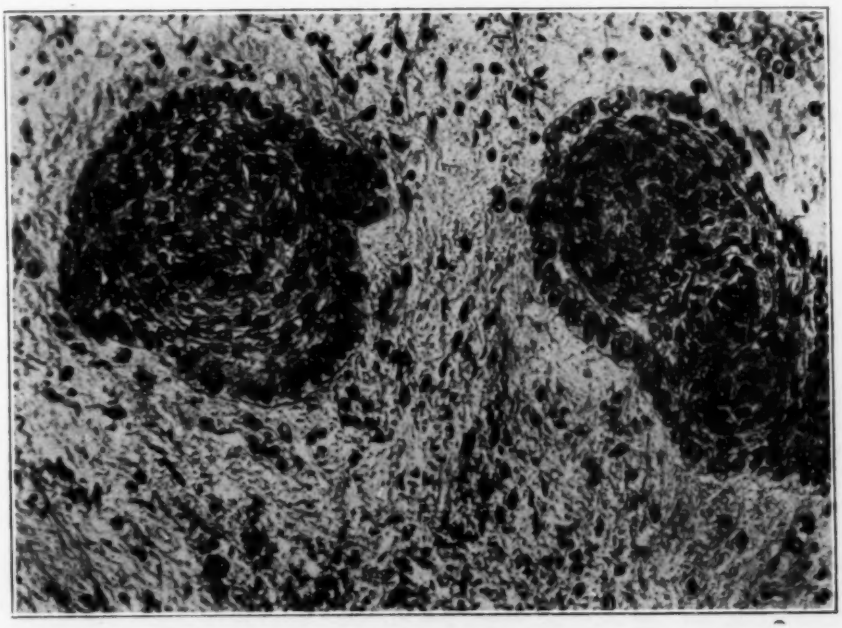

Fig. 7.—Photomicrograph of section from tumor of D. H., Case 2. Two groups of epithelial cells are shown. Neutral ethyl violet-orange G stain. ×850.

Michigan. Early in 1919 he began to have mild headaches in the frontal region. The headaches persisted without much change until four weeks before admission when, following a lumbar puncture, the headaches were greatly aggravated, suboccipital, and projectile vomiting occurred

Examination.—Some suboccipital tenderness and cervical rigidity were present. There was bilateral choked disk with swelling of from 2 to 3 diopters, slight incoordination of the right hand, unsteady gait, and a tendency to fall to the right when the eyes were closed. The deep reflexes were lively, and were exaggerated on the right side. A roentgenogram showed a sella somewhat distorted, but no suprasellar shadow. The visual fields were constricted in the nasal half, the usual binasal defect seen with a receding choked disk.

Operation.—April 1, 1920, Dr. Cushing performed a right subtemporal decompression, during which a ventricular puncture disclosed internal hydrocephalus.

Postoperative Course.— The headaches disappeared and the patient became much more cooperative. April 27, there was noted: nystagmus, more marked on looking to the left; incoordination of all the limbs, especially of the left hand, which showed hypotonicity, hypermetria and tremor; slight equilibratory disturbance, the patient being unable to stand on either foot alone.

Operation.—May 3, 1920, Dr. Cushing performed a suboccipital exploration. Thorough search in midline, recesses, and by puncturing the hemispheres revealed no sign of tumor.

Postoperative Course—The patient did very well after the operation and was discharged May 26. At discharge his headaches were entirely relieved, and the optic disks had receded to 1.5 diopters. He was still very unsteady on his feet, and walked with a wide base. Both decompression areas were flat.

Aug. 3, 1922, the patient was readmitted. In the interval he had done very well. He had an occasional headache and was always somewhat unsteady on his feet, but he went to work and continued to perform it for nearly a year. About a year previous to the second admission, headaches began again and he was at times obliged to stop work and go to bed. He had two or three attacks of vomiting. In the last three months his mentality had begun to change; he was dull and lost interest in his surroundings. During the last month he had commenced to drag the left foot. In the last six months he had gained weight rapidly and had a great craving for candy.

Examination.—The decompressed temporal and suboccipital areas were flat and soft. There were: bilateral secondary optic atrophy; left facial weakness; hemiparesis and hypesthesia on the whole left side of the body; incoordination of the extremities of cerebellar type (dysmetria, hypotonicity, tremor) more marked on the left; equilibratory disturbance with a tendency to fall backward. The deep reflexes were exaggerated on the left, with dorsal toe response and ankle clonus. There was also dorsal toe response on the right. The gait was a curious combination of spastic paraplegia and cerebellar features. A roentgenogram showed the sella to be wide open, rather shallow, and depressed posteriorly. Vision was lost on the left, except for light perception, and the right eye showed the nasal defect of secondary optic atrophy.

Aug. 20, 1922, There being no operative indications, the patient was discharged with a diagnosis of suspected cerebral tumor.

Necropsy.—The patient died at home in September, 1922, and the brain, fixed in 10 per cent. liquor formaldehydi, was sent to us for examination. The third ventricle was filled with a gray, soft, friable tumor (Fig. 8) which projected into the right lateral ventricle, almost filling its middle third. The left lateral ventricle contained only a small portion of the growth (Fig. 9).

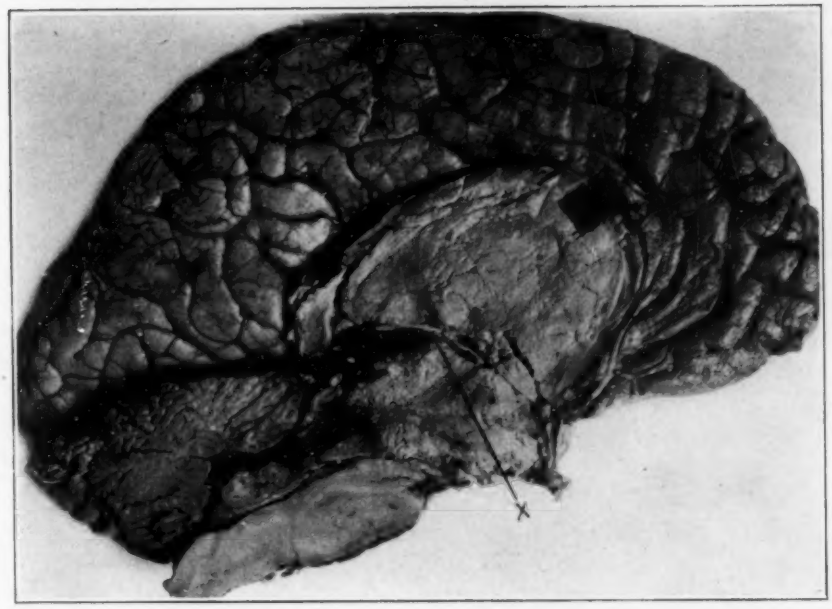

Fig. 8.—Left surface of median sagittal section of brain of R. M., Case 3, showing tumor filling third and fourth ventricles. × indicates the roof of the third ventricle.

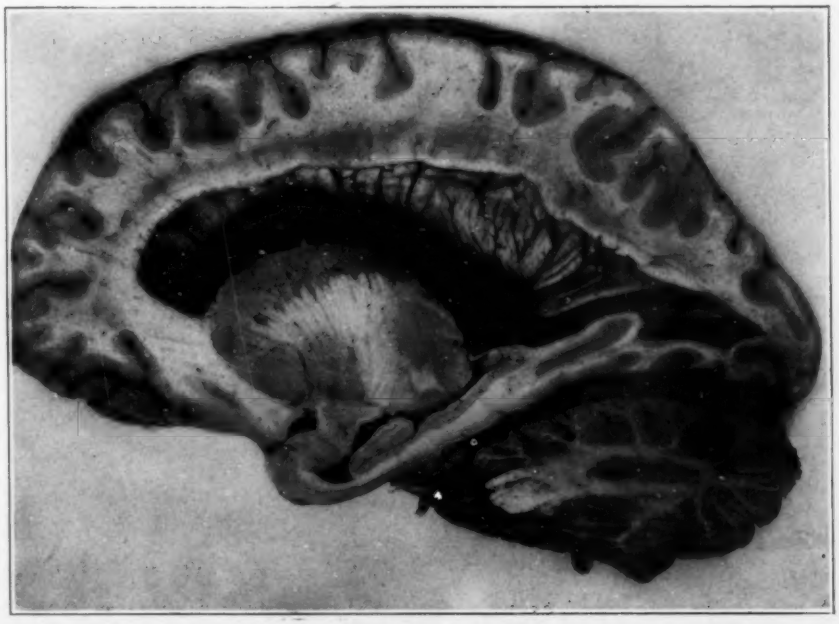

Fig. 9.—Interior of the left lateral ventricle showing tumor bulging into ventricular cavity. Case of R. M., Case 3.

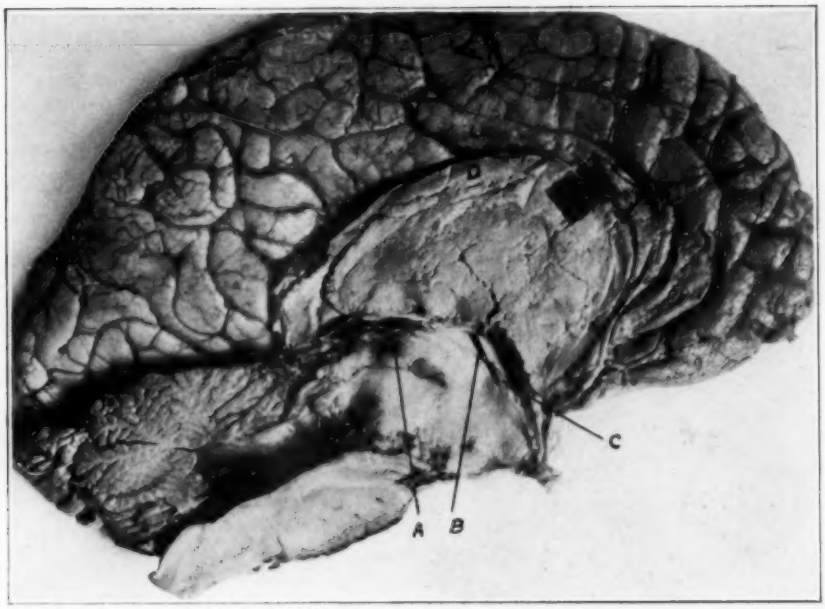

Fig. 10.—Same photograph as in Fig. 8 after the tumor mass has been removed from the third and fourth ventricles. It was nowhere attached to the ventricular walls. Its attachments are seen to be those of the normal septum pellucidum, namely, the corpus callosum, the corpus fornicis, and the columns of the fornix. *A*, corpus fornicis; *B*, foramen of Monro; *C*, column of the fornix; *D*, corpus callosum.

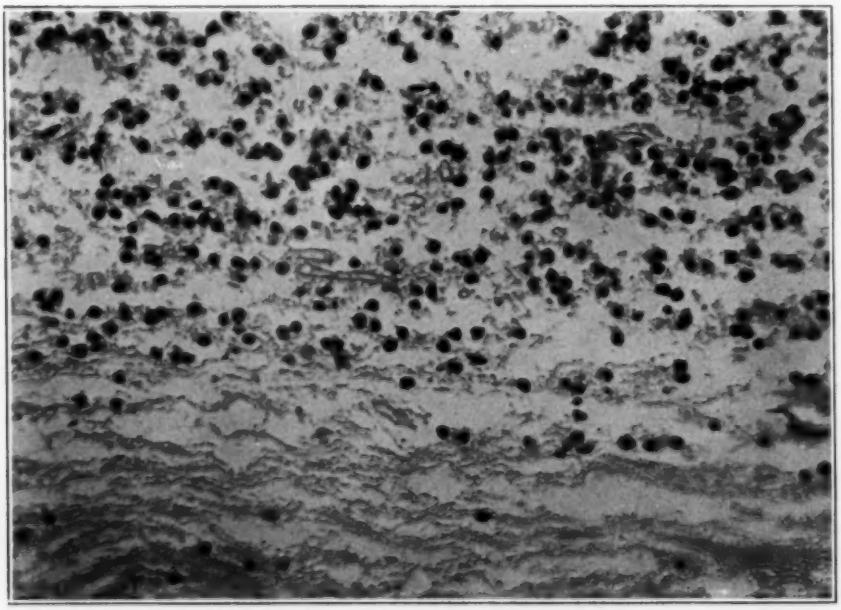

Fig. 11.—Photomicrograph of section of tumor of R. M., Case 3. Section taken from edge of corpus callosum as indicated in Figure 8. Neutral ethyl violet-orange G stain. × 850.

A long finger-like extension filled the fourth ventricle and dilated widely the aqueduct of Sylvius. The neoplasm was not attached to the walls of the ventricles at any point. The choroid plexuses were everywhere free from tumor. It was attached above and anteriorly to the corpus callosum, below and posteriorly to the roof of the third ventricle and the columns of the fornix (Fig. 10). It must, therefore, have arisen from the septum lucidum.

Microscopic Examination.—The tumor was composed of numerous, small, round nuclei, evenly distributed in an indefinite cytoplasmic mass. It is not know how long postmortem the brain was removed. At any rate no details could be determined in the cytoplasm, which remained to all stains an indefinite granular mass (Fig. 11).

COMMENT

The clinical picture produced by a tumor of the cerebellum is usually easy to distinguish from that caused by a suprasellar tumor with its bitemporal hemianopia, primary optic atrophy, genital hypoplasia, etc. But the differentiation is sometimes difficult, as the cases just recorded show, since tumors of the cerebellum may disturb the functioning of the pituitary region by causing hydrocephalus, and, more rarely, suprasellar tumors may disturb the functioning of the cerebellum. Especially is the differentiation difficult when it is impossible to obtain important clinical data because of blindness or lack of cooperation due to youth, stupor or other factors.

The roentgen ray is very useful in the diagnosis of suprasellar tumors. At the present time it can be relied on to show in 85 per cent. of cases the calcification of a tumor of Rathke's pouch. It helps little in the diagnosis of a soft growth such as that described in Case 3.

When there is doubt, great weight must be placed on the chronological order of development of the symptoms, for suprasellar tumors produce cerebellar manifestations by secondary pressure. In each of the three recorded cases the cerebellar symptoms developed late in the clinical course of the disease. On the other hand, cerebellar tumors produce disturbance of cerebellar function by local pressure or destruction of the organ and the symptoms of its derangement are usually present from the onset.

It must not be forgotten, also, that the troubles of equilibration caused by hypertension are probably due to disturbance of the vestibular apparatus (Claude Vincent) and may be distinguished from the disequilibration due to cerebellar lesion by the symptoms proper to derangement of the function of the cerebellum, i. e., hypotonicity, hypermetria, tremor, and so on.

Considering the possible mechanism by means of which the functioning of the cerebellum was disturbed in these patients, it seems most likely that its efferent pathways were involved in the region of the tentorium. In Case 3 an extension of the tumor dilated the aqueduct of Sylvius and projected through it into the fourth ventricle (Fig. 8).

A pocket of the cyst of Case 2 extended through the incisura tentorii into the left cerebellopontile angle (Fig. 6). In both instances the tumor might be supposed to interfere with the superior cerebellar peduncles by compressing them against the edge of the tentorium. It is not clear in Case 1 how this interference occurred. Perhaps here cerebellocerebral connections were interrupted.

At operation, the tumor of Case 1 did not present between the anterior legs of the chiasm, as is usual with these neoplasms, but lay farther back. This may be an explanation of the choked disk, which is not generally associated with these tumors. The same abnormal relationship to the chiasm was seen in another patient with marked cerebellar symptoms but probably it is only a coincidence of no significance for the production of these symptoms.

SUMMARY

The main source of difficulty in the differential diagnosis between supratentorial and infratentorial tumors lies in the equilibratory disturbance which both may cause. Three cases of suprasellar tumor are described which gave rise to symptoms of cerebellar disorder, mainly equilibratory, possibly from interference with the efferent pathways of the cerebellum in the region of the incisura tentorii, or to interruption of cerebrocerebellar connection.

TESTICULAR TERATOMA WITH SECONDARY DEPOSITS IN SPINAL COLUMN AND MENINGES*

FOSTER KENNEDY, M.D., F.R.S.E.

AND

LEWIS STEVENSON, M.D.

NEW YORK

This case is presented because of certain uncommon features in its microscopic examination, some of which explained a confusing clinical picture:

T. C., a man, aged 38 years, was admitted to the Neurological Department, Bellevue Hospital on February 14, and died there thirteen days later. Syphilitic infection occurred at the age of 20. The first symptom of his illness was in October of last year when he experienced a series of severe girdling pains in the distribution of the first lumbar roots. These pains were felt at fairly widely separated intervals up to two weeks before admission to the hospital. He then noticed a weakness of the left leg which in fifty-six hours was useless; paralysis of bladder and rectum followed quickly, and in three more days there was total flaccid paralysis of both lower extremities and of the lower trunk muscles, together with a loss of all sensibility from the level of the fifth dorsal segment downward. There were poorly defined sensory losses above this level.

The abdominal reflexes and those in the legs were abolished. Sacral bedsores speedily developed. The spinal fluid was yellow, most rich in globulin, and two good observers reported 975 leukocytes in each cubic millimeter.

An enlarged left testis was thought to have been the product of an old orchitis. The blood was strongly positive to the Wassermann test. An extensive laminectomy in the lower cervical and upper dorsal region revealed a dry, triangular cord, but no sign of the expected abscess. The patient died on the following day.

Dr. Douglas Symmers performed the necropsy and we are indebted to his courtesy for the necropsy report of which the following is a condensation: The left testis was hard and enlarged; on section a whitish nodule 3 cm. in diameter was found in it. The liver contained several subcapsular whitish areas, and some greenish gelatinous nodules which appeared to be entirely encapsulated. Lying on the left anterolateral aspect of the vertebral column and beneath the pleura was a mass of tissue extending from the second to the seventh dorsal vertebra. It measured 12 cm. long, 8 cm. wide and 7 cm. in thickness. It was deep red, mottled with whitish patches, and soft. The diaphragm was similarly mottled and infiltrated.

The spinal cord in the region of the tenth dorsal vertebra was adherent to the anterior surface of the canal. The bone was here eroded. The spinal tissue below this plane (Fig. 1) was entirely necrotic.

The diagnosis of spinal cord abscess was reached through a consideration of the clinical course and the high count of what were taken

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* Read before the Forty-Ninth Annual Meeting of the American Neurological Association, Boston, May 31, 1923.

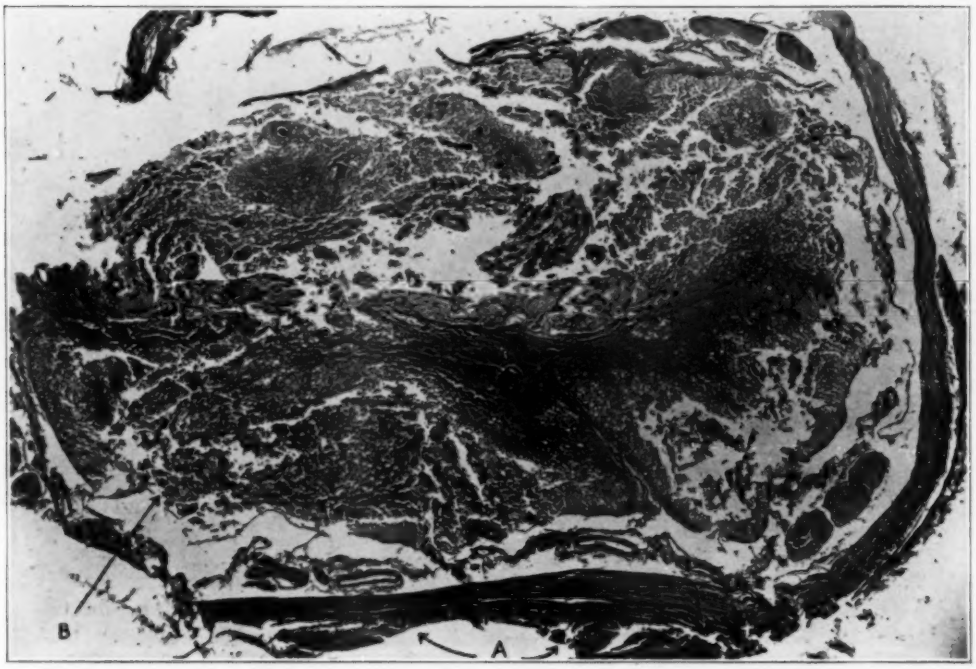

Fig. 1.—Section of cord at ninth dorsal segment; *A*, tumor cells in the dura; *B*, the softened cord.

Fig. 2.—Section of cord at mid-dorsal region: Myelomalacia and cavity formation produced by ascending thrombosis of spinal cord vessels.

Fig. 3.—Section of liver node; *A*, cross section of adult nerve; *B*, tumor cells.

to be leukocytes in the spinal fluid. As we have found no inflammatory changes, we feel compelled to believe these cells were not white blood cells but were cells thrown off by the tumor, or possibly gitter cells. Thrombosis of the venous spinal system explains the degeneration above the level of the tumor (Fig. 2) and excuses, perhaps, our erring locali-

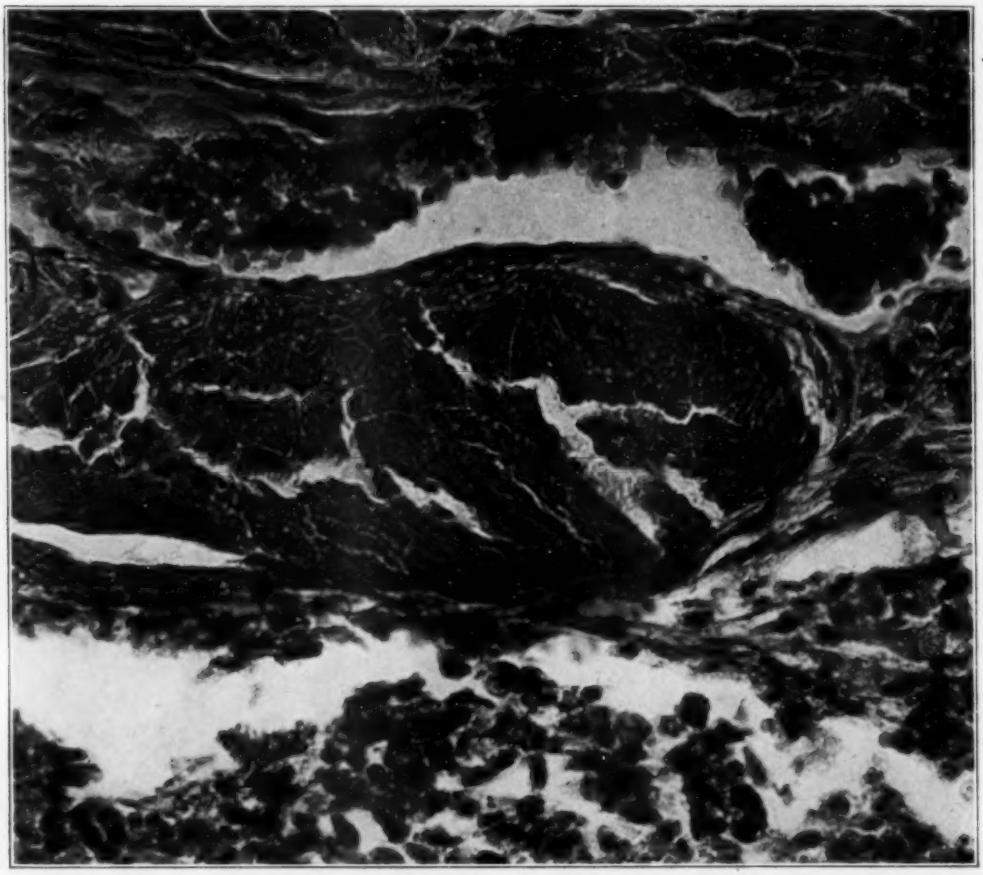

Fig. 4.—A high power magnification of teratomatous theca in which is seen intercalation by tumor cells of the layers of the dura.

zation. The original tumor is far from being uncommon, but in metastases we found one feature of the greatest rarity, namely, nerve fibers of adult type (Fig. 3); further, we have been unable to find any case of testicular tumor metastasis to the meninges of the spinal cord (Fig. 4).

EXPERIMENTS ON THE ETIOLOGY OF RESPIRATORY ARRHYTHMIAS FOLLOWING EPIDEMIC ENCEPHALITIS *

EDWARD C. ROSENOW, M.D.

ROCHESTER, MINN.

The occurrence of pronounced disturbance of respiratory rhythm, often associated with changes in posture and character, following epidemic encephalitis, especially in children, has been reported. The condition is generally regarded as a sequel to the encephalitic attack, as pointed out by Parker in a paper [1] in which he reviewed the literature and reported the findings in eight cases. Owing to certain extremely specific effects which I have observed following the injection of a streptococcus with peculiar neurotropic properties, which has been isolated consistently from cases of encephalitis and epidemic hiccup, I thought that possibly a similar organism might bear etiologic relationship to these strange manifestations. Through the cooperation of Dr. Helmholz and Dr. Shelden, of the Mayo Clinic, I have had opportunity to test this hypothesis.

The technic employed was similar to that used in my studies in encephalitis and epidemic hiccup.[2] Suffice to say that intracerebral or subdural inoculations of suspensions in sodium chlorid solution of nasopharyngeal swabs, and of pus expressed from tonsils, or aspirated from the depths of pyorrheal pockets, and cultures from these, were chiefly employed. Intravenous injections of the respective cultures were made in a smaller number of animals, usually after facilitating penetration of the meninges by subdural injections of sterile water or normal horse serum. Filtrates of washings from the nasopharynx of patients, and of the brains of rabbits that developed typical symptoms, and highly diluted cultures after many rapidly made subcultures were also injected intracerebrally.

FINDINGS IN INDIVIDUAL CASES STUDIED

CASE 1

The clinical findings in this case have been reported by Parker. The patient, a boy, aged 14 years, for one year had had frequently recurring attacks of

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* From the Division of Experimental Bacteriology, the Mayo Foundation.

1. Parker, H. L.: Disturbances of the Respiratory Rhythm in Children, a Sequela to Epidemic Encephalitis, Arch. Neurol. & Psychiat. **8**:630 (Dec.) 1922.

2. Rosenow, E. C.: The Production of Spasms of the Diaphragm in Animals with a Streptococcus from Epidemic Hiccup, J. Infect. Dis. **32**:41 (Jan.) 1923.

hyperpnea, with grunting expirations associated with marked stretching and bending of the trunk and limbs. The symptoms followed an attack of myoclonic encephalitis five months previously.

Experiments.—The effect of intracerebral inoculation of the bacteria in the nasopharyngeal washings was studied in four rabbits, and in the primary culture in two. Of these, five developed markedly increased respiration, which was noisy in two, and also peculiar movements of the head and fore part of the body. A pure, or nearly pure, culture of a green-producing streptococcus was isolated from the brain of each of these rabbits. The streptococcus from the emulsion of the brain of one of these in the primary culture, and in the third, twelfth, and twenty-second rapidly made subcultures was injected into six rabbits and two monkeys, and in the third animal passage into two rabbits. Of the ten animals injected, seven developed symptoms similar to those in the animals injected with the strain in the first passage. Of eight rabbits injected with the strain in the fourth, fifth and sixth animal passages, three developed mild but characteristic symptoms; three died of meningitis during the night, and two remained free from symptoms. The strain injected into the three that developed characteristic symptoms came from a rabbit that died three days after injection, whereas the strain injected into the two that remained free from symptoms came from a rabbit that had been injected ten days previously and had remained well.

Cultures from the brain and blood were made in twenty-two of the rabbits injected intracerebrally with the living organism. Of these, sixteen yielded a pure culture of the green-producing streptococcus from the brain, and five from the blood.

Of the twenty-four animals injected, as shown in the accompanying table, fifteen developed hyperpnea, eleven tremors, nine spasms of muscles, and seven marked ataxia. Spells of noisy, irregular, violent respirations, of varying intensity, often associated with spells of sneezing and coughing, abnormal movements of the head, and alternate raising and lowering of the fore part of the body were the striking picture in fifteen (62.5 per cent.). The tendency of this strain to reproduce the patient's symptoms was noted in two species of animals (rabbit and monkey), and was retained during several animal passages and many rapidly made subcultures. It was lost in both rapid and slow successive animal passage, for as the virulence increased on rapid passage, the animals died of meningitis, and as it diminished on slow passage because of long residence in animals that were recovering and were anesthetized for examination, symptoms did not develop. Thus, of the sixteen rabbits injected in the first three animal passages, twelve (75 per cent.) developed symptoms simulating those in the patient, whereas in the next three animal passages, only three of the eight (37 per cent.) developed symptoms, and in these they were less marked.

Eight rabbits were injected intravenously with the streptococcus in the second animal passage, and two in the third; four were injected with the twelfth rapidly made subculture. Of these, three developed peculiar symptoms (Fig. 3); the others remained well.

Two rabbits were injected with the filtrate of the nasopharyngeal washings, and six with the filtrate of the emulsion of the brain of rabbits that had typical symptoms following injection of the strain in the first, second, and third animal passages. All remained well.

One rabbit injected with 2 c.c. of the spinal fluid remained apparently well for twelve days, and then died. Cultures from the brain and the blood were negative. Sections of the brain showed no lesions.

Illustrative Protocols.—Rabbit 2681, weighing 1,325 gm., was injected intracerebrally May 13, 1921, with 0.1 c.c. of the glucose-brain-broth culture of the nasopharyngeal swab. May 14, at 7:30 a. m., the animal appeared well. At 11:30, it was distinctly unsteady and tremulous; prodding caused markedly increased respirations, and the animal exhibited peculiar contortion-like movements of the head, first pulling it to the right, then up and to the left, and finally flexing it between the fore extremities. At 4 p. m., the peculiar movements of the head and attacks of increased respiration continued; the expirations were forced and audible; spasms of the muscles of the right ear had developed; and the animal ground its teeth. At 10 p. m., the strange movements of the head, associated with attacks of hyperpnea and sneezing spells, were more marked. At 1:30 a. m., the animal was worse. It raised its body to the point of falling backward, breathed audibly, and the sneezing spells recurred at frequent intervals. March 15, at 7:30 a. m., it was found dead. Necropsy revealed marked congestion of the vessels of the meninges, and localized hemorrhages in the pia over the base of the right frontal lobe, and over the medulla and pons. There was no mark at the point of injection. Cultures from the brain yielded a large number of the characteristic streptococcus; those from the blood were sterile.

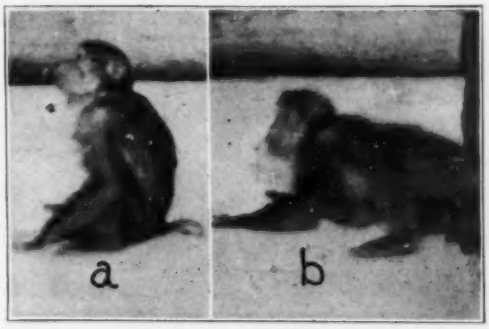
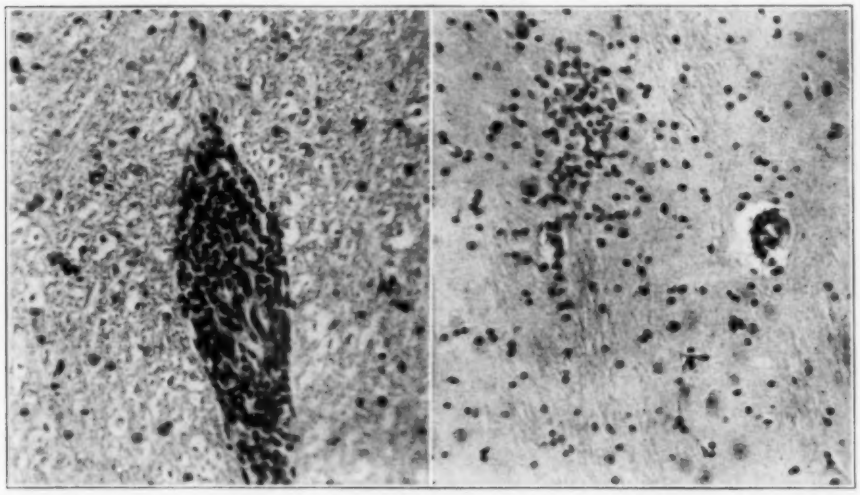


Fig. 1.—*A* and *B*, peculiar postures assumed by Monkey 302 four days after intracerebral injection of the streptococcus after one animal passage.

Monkey 302 was injected intracerebrally May 21, 1921, with 0.3 c.c. of the glucose-brain-broth culture from the brain of Rabbit 2681 after twenty-one rapidly made subcultures (second animal passage). May 22, at 9 a. m., the animal acted peculiarly. It was tremulous and somewhat shaky; it repeatedly crouched, and then rose rapidly on the fore extremities, slowly turning and tilting its head toward the right, and making an expiratory sound. Respirations were irregular in time and amplitude, and moderately increased. May 25, at 8 a. m., the animal acted most erratically. Unsteadiness of the hind extremities was associated with repeated twitching, and clonic spasms of the muscles, especially on exertion. It continued to crouch frequently (Fig. 1*b*), and to bring the body into the erect position, usually tilting the head to the right (Fig. 1*a*), as the respirations became distinctly audible. At 4 p. m., the animal had an attack of extreme restlessness, in which it ground its teeth violently, and assumed various positions. As it raised its body high (Fig. 1*a*) and then crouched to the floor (Fig. 1*b*), marked tremor and occasionally clonic spasms of the muscles of the hind extremities were noted. At 5:15, the animal had a similar attack, in which it looked around wildly, repeatedly had double blepharospasm, crouched

suddenly, leaning to the right (Fig. 1*b*), ground its teeth, and lunged forward, apparently attempting to frighten the observer. At 8 p. m., the strange behavior persisted. May 26, at 7:30 a. m., the abnormal actions were less marked. At 8:30 p. m., there was notable improvement. The animal still acted somewhat peculiarly, ground its teeth moderately, had an occasional blepharospasm, and occasional twitching of the muscles of the upper lip. May 27, it was etherized, and examined at once. The vessels of the pia were markedly edematous and congested, and the cerebrospinal and ventricular fluids were slightly turbid. There were no lesions of the cranial nerves, and no gross hemorrhages in the brain or cord. Cultures of pipetted material from the brain yielded a pure growth of the characteristic streptococcus; those from the spinal fluid and blood were negative.

Sections showed moderate perivascular leukocytic and round-cell infiltration in the meninges of the sulci over the cerebrum, the pons, and the medulla, and



A B

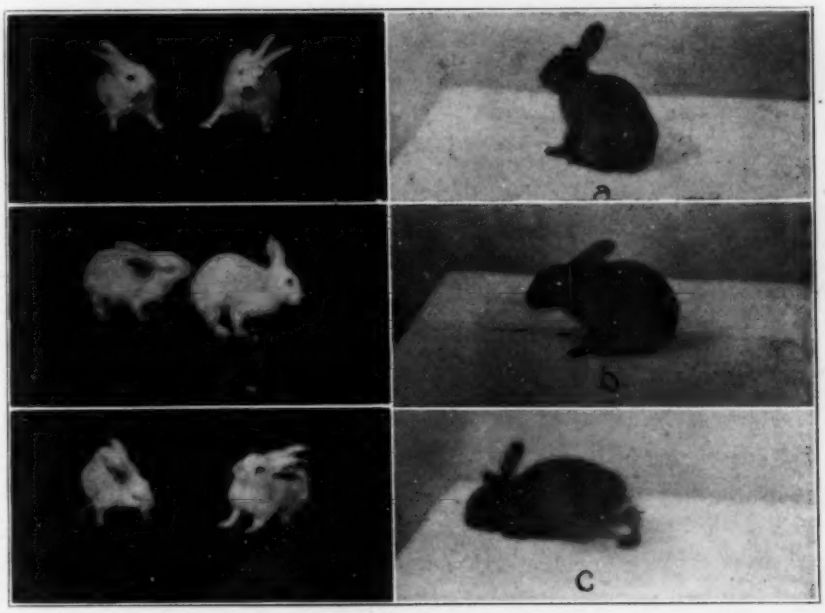
Fig. 2.—*A*, perivascular infiltration in the pons of Monkey 302; *B*, adventitial and localized round-cell infiltration in the lateral anterior aspect of the medulla in Monkey 302. Hematoxylin and eosin, × 120.

several areas of perivascular and localized infiltration in the lateral aspect of the medulla (Fig. 2) and diplococci in the lesions (Fig. 14, *a*, *b*).

The results on intravenous injection of the strain from Rabbit 2681 in the third subculture are illustrated in the following protocol:

Rabbit 2707, weighing 580 gm., was injected May 16, 1921, with 5 c.c. of the glucose-brain-broth culture in the third rapidly made subculture. May 17, the animal appeared well. May 18, at 7 a. m., it moved its head from side to side at frequent intervals. At 12 m. the movements of the head had changed. It was brought slowly to the right and downward, the nose touching the floor, and then suddenly pulled into normal position, and again to the right, as the body was raised high on the fore extremities. Respirations were moderately increased. At 10 p. m., the condition was unchanged. May 19, the animal ate carrot with relish. The peculiar movements had changed. The head and fore

part of the body were raised (Fig. 3 *Aa* left), brought to a more normal position with head extended (Fig. 3 *Ab*), and then lowered as the head was flexed (Fig. 3 *Ac*), often low between the fore extremities. The respirations were somewhat irregular and moderately increased. This condition continued until May 24, at 4 p. m., when the animal was found dead. The findings at necropsy were negative. Cultures from the blood remained sterile, whereas those from the brain yielded a pure growth of the streptococcus. Similar results were obtained in two rabbits injected with the strain from Rabbit 2681 after twelve rapidly made subcultures. The various postures of one were almost identical with those of Rabbit 2707 (Fig. 3*A*, right), and those of the other simulated closely the movements of the patient (Fig. 3*B*).



A B

Fig. 3.—*A*, peculiar postures of two rabbits injected intravenously with the streptococcus after one animal passage, one (left) in the third, the other (right) in the twelfth, rapidly made subculture. Note the marked similarity of the postures; *B*, peculiar postures assumed by rabbit injected intravenously with the streptococcus in the second animal passage and the twelfth rapidly made subcultures. Note the elevated position of the fore part of the body and the crouched position.

The lesions in these rabbits following intravenous injection consisted of slight but widely disseminated perivascular and localized infiltration by round cells, most marked in the medulla and pons (Fig. 4), and diplococci in the lesions (Fig. 14 *c*).

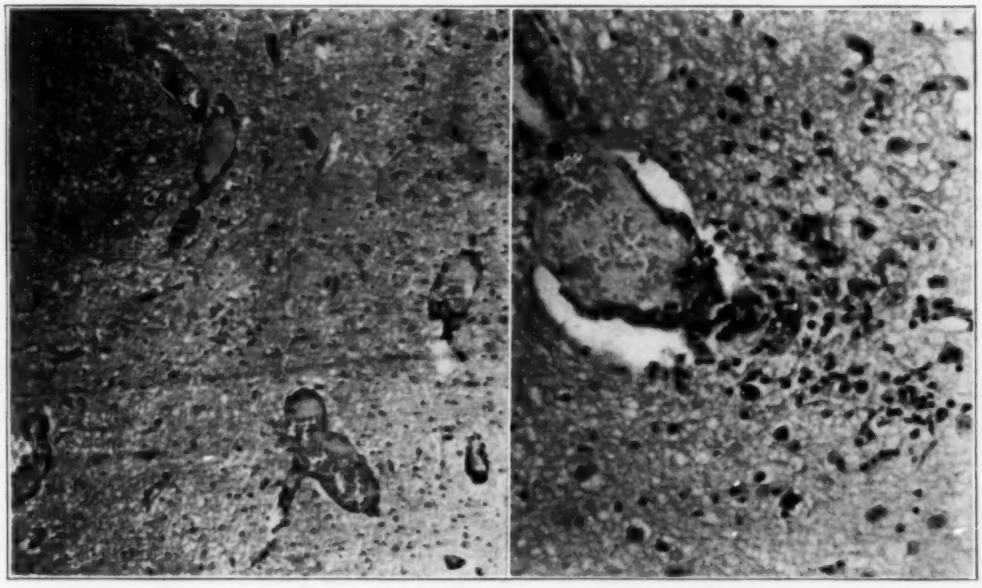
CASE 2

The detailed clinical findings in this case have also been reported by Parker. The patient, a girl, aged 12 years, soon after an attack of influenza two years previously, had developed marked change in character, noticeable in her facial

expression and posture (Fig. 5*A*), associated with alternate attacks of apnea, in which she threw her head back sharply (Fig. 5*B*), and noisy, forced respirations as the head was brought forward.

Experiments.—The effect of the streptococcus obtained from the nasopharynx of this patient was tested by inoculating the washings from the swab, the emulsion of the brain of positive rabbits and after five animal passages, and cultures in glucose-brain-broth as high as the fifty-third rapidly made subculture.

Of the twenty-five animals (twenty-three rabbits and two monkeys) injected, twenty-three developed marked hypernea, often associated with alterations in rhythm, expiratory sounds, and spasmodic coughing and sneezing spells; twelve developed retraction of the head, ten tremor of muscles, five nystagmus, two spasms of the diaphragm, three spasms of abdominal and other muscles,



A B

Fig. 4.—*A*, adventitial and perivascular infiltration by round cells in the medulla of rabbit shown in Figure 3*A* (right), four days after intravenous injection of the streptococcus after one animal passage and twelve rapidly made subcultures; *B*, adventitial and localized infiltration by round cells in the pons. Hematoxylin and eosin, × 150.

seven marked weakness, and nine ataxia. The respiratory syndrome was noted in both of the monkeys injected with the strain after one rabbit passage. The two rabbits in which no symptoms were noted died during the night after inoculation with the strain after two and three animal passages, respectively.

The paroxysmal attacks of extreme and noisy respirations became less marked and less frequent as the duration of the experiments became shorter from consecutive animal passage. This was also true as the strain was rapidly subcultured. In both instances meningitis and paralytic symptoms became greater. Intraperitoneal injection into mice and intratracheal inoculation in

guinea pigs were without effect. Two rabbits injected intracerebrally with 1.5 c.c. of the filtrate of the emulsion of the brain of one positive rabbit in the first animal passage remained free from symptoms.

Cultures from the brain and the blood were made in twenty-three of the twenty-five animals. The green-producing streptococcus was isolated from the brain in twenty-two, from the blood in eight. The incidence of this organism in the blood became greater as the virulence increased, cultures being positive in only two of nine rabbits injected in the first two passages, and in six of fourteen injected in subsequent passages.

A B

Fig. 5.—Peculiar facial expression and posture of the patient in Case 2.

Illustrative Protocols.—Rabbit 3252, weighing 1,650 gm., was injected Jan. 24, 1922, intracerebrally with 0.1 c.c. of the sodium chlorid solution of the washings from the nasopharynx of the patient. January 25, at 8 a. m., it was found in the cage with the fore part of the body elevated and the head retracted. The respirations were markedly increased, and associated with prolonged intervals of expiratory groans, and spells of sneezing. At 11 a. m., the condition was about the same, except that the intervals of noisy breathing were shorter and recurred more frequently. At 10 p. m., the animal was extremely restless. It breathed more violently, repeatedly raising and flexing the head, and nystagmus and tremor of the fore part of the body had developed. January 26, at 8 a. m., it

was found dead. The meninges were moist and hyperemic; the ventricular and spinal fluids were slightly turbid; the pia over the anterior part of the medulla was edematous and infiltrated; and the lungs were moderately edematous. There were no lesions in other organs, and none in the diaphragm, nor phrenic, vagus, or sympathetic nerves. There was no mark at the point of injection, and no gross hemorrhages anywhere. Cultures from the brain yielded a large number of colonies of the streptococcus; those from the blood a few colonies.

A B

Fig. 6.—Rabbit 3341 injected intracerebrally with the highly diluted culture of the streptococcus from the patient in Case 2 after one animal passage and forty-seven rapidly made subcultures.

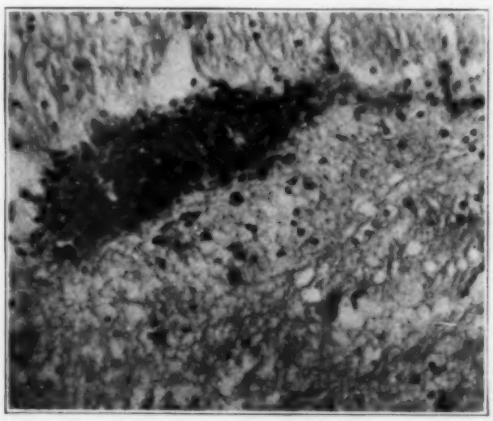


Fig. 7.—Perivascular infiltration in the brain of rabbit shown in Figure 6.

Monkey 321 was injected intracerebrally Jan. 27, 1922, with 0.1 c.c. of the glucose-brain-broth culture of the brain of Rabbit 3252. January 28, it appeared well until 9 p. m. At this time the respirations were markedly increased and audible even when the animal sat quietly in the cage. When lifted from the cage, and after running about, the respirations, from fifty to seventy-five each minute, were so audible and so marked that they could be heard outside the

room. January 29 and 30, the respirations were still notably increased, especially after slight exertion. The animal felt hot; there was inequality of pupils, but no nystagmus, no peculiar motions of the head, no tremor, nor apparent weakness. January 31, when the animal was quiet in the cage, the respirations were only moderately increased, but on slight exertion they became extremely marked and could be readily heard at a distance of ten feet. This condition continued until February 10, when the animal was chloroformed. No gross lesions were found. Cultures from the emulsion of the brain yielded a pure growth of the streptococcus; those from the blood were sterile.

Sections showed slight neurophagocytosis of ganglion cells, and perivascular round-cell infiltration in the pons and medulla.

Rabbit 3341, weighing 1,430 gm., was injected intracerebrally Feb. 14, 1922, with 0.2 c.c. of a 1:1000 dilution of the glucose-brain-broth culture of the streptococcus from the brain of Rabbit 3252 after forty-seven rapidly made subcultures. February 15, at 8:45 a. m., the respirations were increased. The animal was disinclined to hop, and hopped awkwardly when made to do so. At 4 p. m., there was marked disturbance of respiration. The animal held its head high for long periods, during which the respirations became shallow and slow; then from no apparent cause, it would bring its head forward, breathing violently, as it tended to lose its balance. At 7 p. m., the condition was unchanged. February 16, the animal sat quietly in the cage, usually with the head high, and ground its teeth repeatedly. It was disinclined to move, and sometimes appeared to fall asleep. When pushed forward, it tended to lose its balance, and repeatedly brought its head sharply forward and markedly backward. Respirations were only moderately increased, but varied considerably in rhythm and amplitude. February 17, the animal appeared well, but the movements of the head persisted. The respirations were normal, but on exertion became much exaggerated. It repeatedly brought its head far backward, even to the point of falling over its haunches. February 18, in attempting to take a photograph of the animal with its head in normal (Fig. 6*A*) and in markedly retracted positions (Fig. 6*B*), it was found that if an object was brought slowly down over the head, without touching the nose, the head would be held in a normal position long enough to be photographed. This occurred on repeated tests. Occasionally the animal appeared stubborn and refused to bring its head into normal position even if the nose was touched. Following this, the respirations became normal, but the movements of the head persisted. There were periods when it was held in a normal position, and others when it was held in retracted position almost continuously, and brought forward only long enough to enable the animal to take food. March 20, it was found dead, apparently from intercurrent cause. Cultures from the brain and the blood were sterile.

Sections revealed perivascular round-cell infiltration in the pia over the pons, and an area of round-cell infiltration in the subcortical region in the left hemisphere (Fig. 7).

The emulsion of the brain of Rabbit 3252, from which the culture injected into this rabbit was isolated, produced retraction of the head in one rabbit, and lateral movements in another (Fig. 8), associated in both with marked respiratory disturbance.

CASE 3

The patient, a boy, aged 6 years, after an attack of encephalitis one year before my study, became abusive, had bursts of passion, and developed alternating attacks of apnea and constant noisy breathing, often falling unconscious at the climax of these actions. The detailed clinical findings in this case have been reported by Parker.

Experiments.—Eight animals (seven rabbits and one monkey) were injected with the streptococcus from this patient, three directly with varying doses of the suspension in salt solution of the swab from the nasopharynx, and five with the strain obtained from the brain of two of these animals. Six of the animals developed hyperpnea, usually associated with spells of marked arrhythmia and spasmodic respirations, two spasms or twitchings of muscles, two weakness, and two convulsions. Cultures from the brain yielded a pure culture of the streptococcus in seven, those from the blood in four of the eight.

Two rabbits were injected with the filtrate of the fresh emulsion of the brain of one of the rabbits which developed marked symptoms following injection of the suspension from the throat. Both remained free from symptoms, and were anesthetized twelve days later. Cultures from the brain and the blood remained sterile, and sections were negative.

The effect of intranasal inoculation of this strain was tested by packing the nose of four rabbits with gauze soaked in the culture. In two, respiratory symptoms developed, but these were less marked than following intracerebral

Fig. 8.—Rabbit injected intracerebrally three days before with the brain emulsion of Rabbit 3252 (Case 2). Note the lateral position of the head.

inoculation. Death occurred in nine and eighteen days respectively, and cultures were negative. One died in forty-eight hours, with large numbers of the organism in the brain and the blood, and one died in five days from snuffles.

Illustrative Protocol.—Rabbit 3261, weighing 1,270 gm., was injected intracerebrally Jan. 26, 1922, with 0.1 c.c. of the sodium chlorid suspension of the washings from the nasopharynx of the patient. January 27, at 8 a. m., the respirations were moderately increased. The animal sat quietly most of the time, but occasionally ran to the opposite side of the cage and crouched to the floor, the respirations becoming markedly increased. At 10 a. m., expiratory groans had developed. At 4 p. m., the condition was about the same. The animal often crouched suddenly and then ran to the opposite corner of the cage in an excited manner. Following these attacks, it repeatedly brought its head sharply under its body and bit its right fore paw vigorously. Several times after one of these attacks it grasped a mouthful of excelsior from the floor of the cage, turned completely over, and developed a series of clonic spastic movements of the extremities, following which it assumed a normal position, breath-

ing quietly but vigorously. At 9 p. m., it was found in the cage in a crouched position, breathing violently. While being watched, it suddenly raised the fore part of the body high, apparently excited, held its breath for a moment, developed severe clonic spasms of the muscles, abruptly threw its head under its body, attempted to bite its foreleg and the fur on its chest, fell to the side, developing terrific spasms of the muscles of the back, and flexed its head sharply forward, with prolonged and forced expiration. January 28, at 8 a. m., the animal was found dead. There were marked congestion of the vessels of the meninges and edema and infiltration of the pia on the anterior aspect of the medulla; the brain and cord were soft. There were no gross hemorrhages in the brain, cord, the vagus or sympathetic nerves, nor ganglia. The cultures from the brain and the blood yielded a pure growth of the streptococcus.

CASE 4

A girl, aged 13 years, came to the clinic Feb. 17, 1922, on account of a feeling of suffocation which had persisted for two and one-half weeks. Her appendix had been removed about five months previously. The suffocating attacks occurred both day and night, and often awakened and frightened the patient. This was associated with cardiac disturbance, due to palpitation. One month before our examination, she had had a peculiar attack of deep breathing, which lasted for several hours.

Examination.—The respirations were more or less continuously forced, averaging fifty each minute. The abdomen was drawn in markedly with each inspiration, and pushed out with each expiration. The patient had had frequent attacks of tonsillitis three years prior to coming to the clinic. The child was well nourished; the leukocytes numbered 6,300; the pupils were equal and reacted to light and in accommodation; the fundi were normal; the tonsils were moderately enlarged, and infected; the cervical lymph glands were palpable; there was moderate tenderness in the region of the appendix, presumably due to postoperative adhesions.

Experiments.—Characteristic symptoms were produced in animals with the strain obtained from the pus expressed from the tonsils. This occurred in three of five rabbits injected with the strain in the first and second animal passages. Two rabbits were injected with the strain after seventeen subcultures. Of the seven animals injected, four developed hyperpnea as a striking symptom, four tremors, two ataxia, and one each lethargy, paralysis, spasms of muscles, and rhythmic movements. Cultures were made of the brain and the blood in five. Green-producing or slightly hemolyzing colonies of streptococci were isolated from the brain in three and from the blood in one.

The filtrate of the emulsion of the brain of one of the positive rabbits was injected intracerebrally into four rabbits. All remained free from symptoms.

Illustrative Protocols.—Rabbit 3372 was injected intracerebrally Feb. 20, 1922, with 0.2 c.c. of a salt solution suspension of the nasopharyngeal swab. February 21, at 8 a. m., the animal was found in the cage with seven other rabbits that had been similarly injected with material from sources other than respiratory arrhythmia. It was easily distinguished by the marked increase in respirations. It appeared well otherwise. At 9 a. m., the hyperpnea continued, and the animal was slightly tremulous when forced to hop. At 12 m., the respirations were still markedly increased, and it was noted that with each respiration the chest wall contracted as the abdominal walls expanded. At 3 p. m., the condition was much the same. February 22, at 8 a. m., the animal sat quietly in the cage, with notable increase in rate and amplitude of respiration. When

made to hop, decided tremor of the fore part of the body and extremely marked respirations developed. February 23, at 8 a. m., it was found sitting at the side of the cage with decidedly increased respiration, marked tremor of the fore part of the body, and moderate weakness. At intervals the respirations became irregular, and the animal had difficulty in breathing, apparently on account of spasmodic closure of the glottis. At 9 a. m., it was found dead. Necropsy revealed marked congestion of the vessels of the meninges, and edema of the pia at the upper pole of the medulla. Cultures of the brain and the blood yielded a pure growth of the streptococcus. Sections showed marked leukocytic and beginning round-cell infiltration, especially on the anterior aspect of the medulla.

Rabbit 3428, weighing 1,440 gm., was injected intracerebrally March 4, 1922, with 0.2 c.c. of a 1:1,000 dilution of the glucose-brain-broth culture of the brain of Rabbit 3372 after seventeen rapidly made subcultures. March 5, the animal appeared well. Respirations were normal, but moderate ataxia had developed. March 6, the respirations were increased, ataxia was more marked, and peculiar movements of the head had developed. March 7, the animal sat quietly as if half asleep. It could be aroused readily, and when made to hop, peculiar tic-like movements of the head, marked ataxia, and increased respirations developed. March 8, the condition was about the same. The animal was observed until March 27. The movements of the head continued, and weakness of the hind extremities gradually developed. It was anesthetized for examination. No gross lesions were found. The brain and blood were sterile. Sections showed slight perivascular round-cell infiltration in the basal nuclei; sections of the lumbar cord were not made.

Four days after the first series of experiments, the patient's tonsils were removed. An emulsion was made and three rabbits were injected, with negative results.

CASE 5

A woman, aged 27 years, came to the clinic Feb. 16, 1922, on account of extreme nervousness associated with jerky respirations and peculiar movements of the muscles throughout the body, resembling a general tic. She had had repeated hysterical attacks following a nervous shock, associated with a sexual background.

Examination.—The patient appeared childish, carried a story book and "funny" papers. She was extremely restless, moved around the room, picked up objects, only to throw them to the floor, breathed noisily, and complained of difficulty in getting her breath, often going to the open window. The nasopharynx was hyperemic; the tonsils were submerged and infected; the teeth were normal; the Wassermann reaction was negative; the urine was normal; the leukocyte count was 9,000, and hemoglobin 69.

Experiments.—The two rabbits injected with the salt solution suspension of the nasopharyngeal swab developed almost identical symptoms, which resembled somewhat those in the patient.

Illustrative Protocols.—Rabbit 3376, weighing 2,000 gm., was injected intracerebrally Feb. 21, 1922, with 0.2 c.c. of a sodium chlorid solution suspension of the nasopharyngeal swab. February 22, at 8 a. m., the animal sat quietly in the cage. It appeared well, but was unsteady in hopping; the respirations were jerky and moderately increased and became readily audible when it was prodded. These symptoms continued throughout the day. February 23, at 8:30 a. m., the respirations were less marked when the animal was quiet. On exertion,

it became abnormally excited, held its ears far forward, breathed in jerky fashion at intervals, and developed clonic contractions of the muscles of the trunk and the extremities. These symptoms were almost paralleled by those of its mate, which had been injected in the same way. February 24, it appeared well when quiet in the cage, but when prodded it became tremulous, and the respirations again became jerky and rapid. It was anesthetized for examination. Cultures from the brain yielded a pure growth of the streptococcus; the blood was sterile. Sections revealed marked leukocytic and round-cell infiltration, chiefly on the anterior aspect of the medulla, and many gram-positive diplococci in the lesions.

The monkey injected developed a curious train of symptoms, which in some respects also resembled those in the patient.

Monkey 317 was injected intracerebrally Feb. 21, 1922, with 0.8 c.c. of a sodium chlorid solution suspension from the nasopharynx of the patient. February 22, at 8 a. m., it appeared well. At 10 a. m., the animal had a peculiar attack of generalized clonic contractions of the muscles in which it

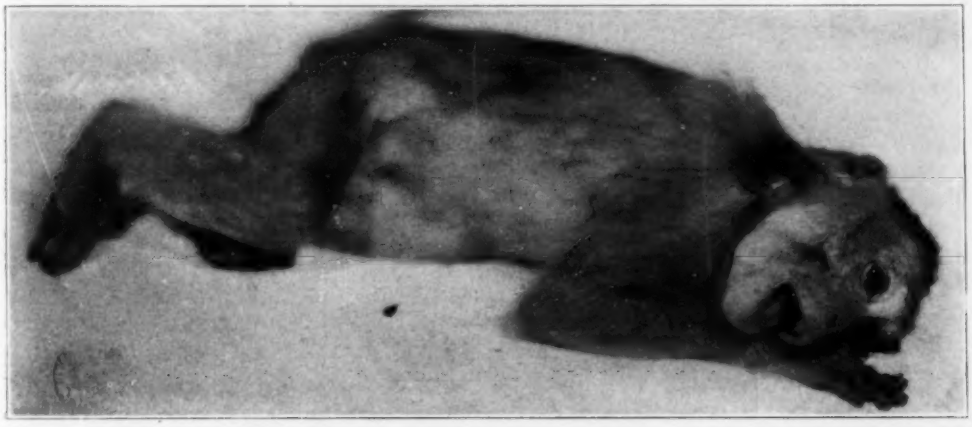


Fig. 9.—Monkey 317 injected three days previously with the streptococcus from the patient in Case 5. Note the peculiar crouched position, the open mouth, and the staring, dazed expression.

clung tightly to the screen door of the cage, held its breath until it became markedly cyanosed, and then relaxed, losing its hold. Slight prodding provoked another attack. On relaxation the respirations became marked and irregular, and, as the animal opened its eyes, twitchings of the eyelids and rapid horizontal nystagmus in both eyes and clonic spasms of the muscles of the extremities developed, after which it appeared confused. It remained quiet most of the day. At 8 p. m., it acted peculiarly, was a little unsteady, and tended to miss its mark in climbing to the perch. February 23, it was erratic, often crouching to the floor of the cage, moving in a shuffling manner, turning its head to the left, leaning to the side of the cage, and looking at the wall in a dazed fashion. When lifted from the cage and placed on the floor, it repeatedly crouched, then slowly got on its feet, and moved in a circle constantly to the left. It was alert and noticed slight movements and sounds. In the forenoon, it ate bread, but in the afternoon it did not do so, and acted peculiarly. It opened its

mouth widely and held it open when pieces of bread were placed in it, but did not bite the bread. When it was removed, the animal opened and closed its mouth slowly a number of times. There was increased tonus and coarse tremor of the muscles of the extremities. During one period of observation, after being thoroughly aroused, it ate bread normally, and picked bread crumbs from the floor, placing them in its mouth. While doing this, it suddenly looked from side to side, repeatedly crouched, turned its head, opened its mouth and eyes, and stared as if bewildered (Fig. 9). February 24, it was found dead. There were moderate congestion of the vessels of the meninges, marked congestion of the vessels on the anterior part of the medulla and pons, and a small area of softening at the point of injection. Cultures of the brain yielded a pure growth of the streptococcus; those from the blood were sterile. Sections revealed perivascular hemorrhages and round-cell infiltration in the pons adjacent to the third ventricle, and diplococci in lesions (Fig. 14 *d*).

Fig. 10.—Peculiar dazed expression and turning of the head to the left at the end of the periods of alternating hyperpnea and apnea, patient in Case 6.

CASE 6

A boy, aged 17 years, came to the clinic March 8, 1923, because of peculiar respiratory difficulty. He had been well until Feb. 21, 1922, when he had an attack of what appeared to be influenza. Following this, he developed a peculiar cough, for which, in July, tonsillectomy was performed and the uvula clipped, with only temporary relief.

Examination.—He had paroxysms of coughing, lasting from two to five minutes, which really were expiratory grunts with each respiratory cycle. After these attacks, his head turned to the left, his mouth was held open, his tongue rolled, and he seemed dazed (Fig. 10). Intervals of apnea and hyperpnea alternated (Fig. 11), expiratory grunts occurring with each expiration. General examination was largely negative. The teeth were normal, the tonsils had been cleanly removed. The nasopharynx was hyperemic and covered with a moderate amount of mucopurulent material.

Experiments.—The effect of intracerebral injection of the streptococcus from the nasopharyngeal swab was studied in nine rabbits. Symptoms resembling those noted in the patient, paroxysmal cough, sneezing spells, and peculiar movements of the head, developed in seven. Two were injected with the suspension in sodium chlorid solution of the throat swab, three with 0.1 c.c. of the undiluted primary culture from the throat, 0.1 c.c. of a 1:100 dilution, and 0.1 c.c. of a 1:1,000 dilution, and two with the culture of the dried brain of a positive rabbit one month later. Two were injected with the strain in the second animal passage after seventeen rapidly made subcultures. One of these, receiving 0.1 c.c., died during the night; the other received 0.1 c.c. of a 1:1,000 dilution of the same culture, lived for three days, and developed peculiar movements of the head, increased respiration, and marked lethargy.

Of the nine rabbits injected with the living streptococcus (Tabulation), eight developed hyperpnea, five peculiar turning of the head, four tremors,

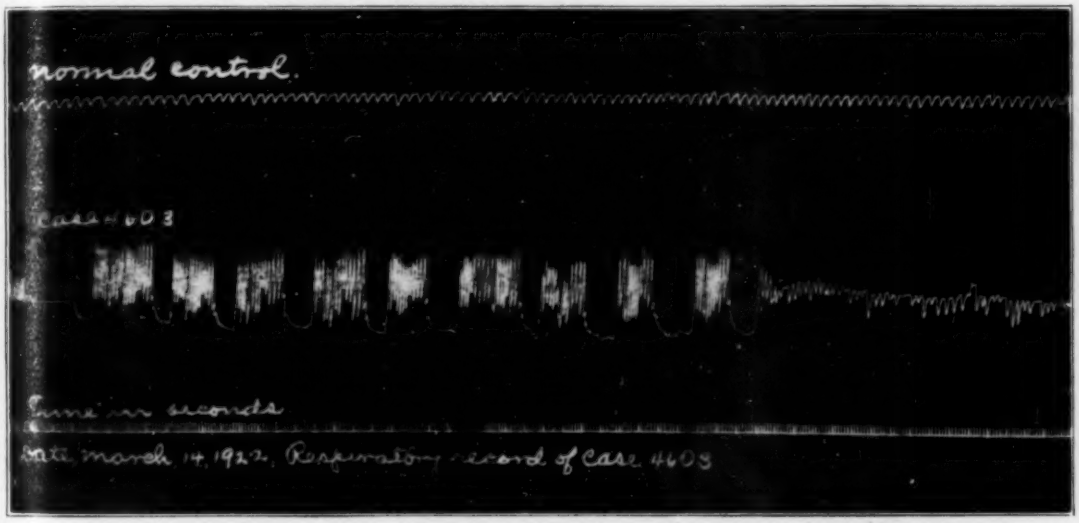


Fig. 11.—Respiratory record illustrating alternating periods of hyperpnea and apnea (Case 6), with normal control.

three extreme weakness, two twitchings, and two ataxia. Cultures from the brain of eight of the rabbits injected yielded the streptococcus in five, those from the blood in two. A few staphylococci were isolated from the brain with the streptococci in four instances, and from the blood in two.

Two rabbits were inoculated with 1.5 c.c. of the filtrate of the nasopharyngeal washings. Both remained well.

Illustrative Protocols.—Rabbit 3456, weighing 1,770 gm., was injected intracerebrally March 13, 1922, with 0.2 c.c. of a sodium chlorid solution suspension of the nasopharyngeal swab. March 14, it sat quietly in the cage, with the fore part of the body raised (Fig. 12 *B*). It frequently brought its head rather sharply but slowly to the left (Fig. 12 *B*), synchronous with marked clonic twitchings of the masseters. Respirations were markedly increased. At 10 a. m. the condition was about the same, but paroxysms of sneezing and coughing had

developed. At 2 p. m., these paroxysms were more violent. The respirations were more irregular (Fig. 13), and the head turned more frequently. The symptoms increased rapidly in severity, and the respirations could be heard at a distance of ten feet. At 4:35 p. m., during a paroxysm of hard breathing, the respirations suddenly ceased and the animal died without a struggle.

A B

Fig. 12.—Rabbit 3456 (*B*) and mate (*A*), showing lateral turning of the head, following injection of the streptococcus from patient in Case 6.

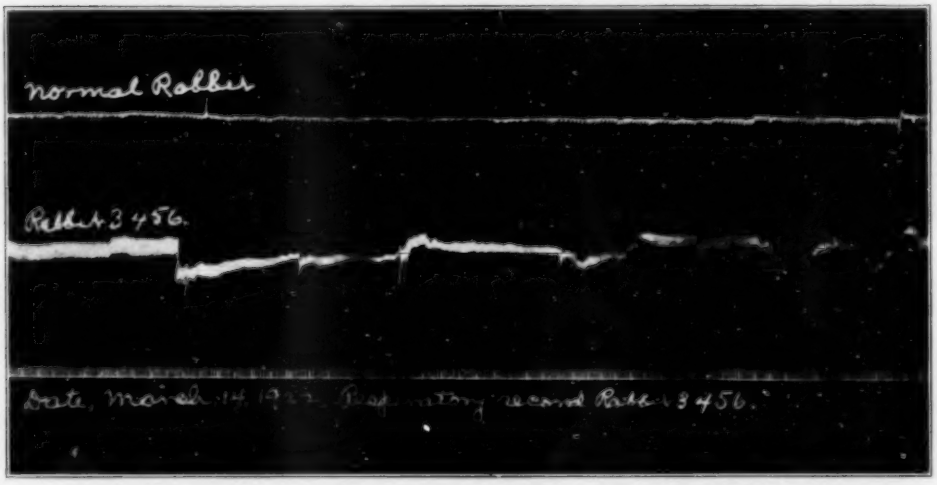


Fig. 13.—Respiratory record of Rabbit 3456 showing extreme respiratory arrhythmia, together with normal control.

Necropsy disclosed moderate congestion of the vessels of the meninges, numerous small hemorrhages on the posterior aspect of the medulla, and edema and infiltration of the pia on the upper pole of the medulla. Cultures from the brain yielded a large number of colonies of the streptococcus, those from the blood a small number.

The mate to this rabbit (Fig. 12 *A*) developed an almost identical train of symptoms. Sections of both revealed perivascular and localized hemorrhagic and leukocytic round-cell infiltration and easily discoverable diplococci in the lesions (Fig. 14 *e*).

Rabbit 3522, weighing 1,520 gm., was injected intracerebrally March 20, 1922, with 0.2 c.c. of a 1:1,000 dilution of the glucose-brain-broth culture of the strain from Rabbit 3456 after fourteen rapidly made subcultures. March 21, at 7 a. m., vertical nystagmus, with synchronous movements of the eyelids, tilting of the head to the right, ataxia, and markedly increased respirations had developed. At 11 a. m., the ataxia and nystagmus were moderately improved, but the respirations were more labored. At 3 p. m., it was more quiet and repeatedly appeared to fall asleep, the head drooping slowly to the point of touching the floor, when it was suddenly thrown backward. At 9:30 p. m., the condition was unchanged. March 22, the respirations were less marked and the animal was quiet, apparently asleep most of the time. March 23, it was

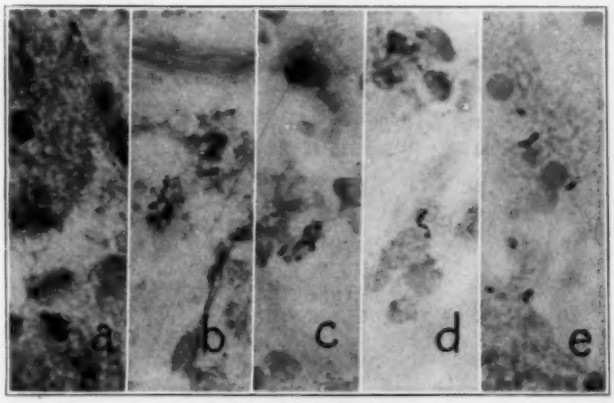


Fig. 14.—Diplococci in the lesions of the brain of animals; *a* and *b*, Monkey 302; *c*, Rabbit 2721; *d*, Monkey 317; *e*, Rabbit 3456, injected respectively six, four, three and two days previously.

found dead. There were marked congestion of the vessels of the meninges and slight turbidity of the cerebrospinal fluid. A pure growth of the streptococcus was obtained from the brain; the blood was sterile.

CASE 7

A girl, aged 4½ years, was brought to the clinic April 17, 1922, on account of attacks of alternating apnea and hyperpnea, which followed what was considered influenza four weeks previously. After the periods of apnea, the breathing was quiet and slow, then became noisy, more rapid, and deeper with each succeeding breath up to a climax, when she opened her mouth, made grimaces, and her hands twitched and writhed. She had strength in both arms, but did not use the left arm. She walked with legs wide apart, stiff and stilted. They seemed spastic, and the gait was unsteady. She took little interest in surroundings, and sat quietly, breathing noisily in a peculiar fashion. She drooled saliva, and continually held the fingers of her left hand in her mouth. Her teeth were normal; the tonsils were large and infected; the cervical glands

were palpably enlarged; the temperature was 99.6; hemoglobin was 55; erythrocytes 3,560,000, and leukocytes 10,400. The blood Wassermann and Pirquet reactions were negative. The biceps reflexes were increased. She had apparently had an attack of encephalitis at 1½ years of age.

Experiments.—Seven rabbits were injected with the living streptococcus from the nasopharynx, two with the suspension in sodium chlorid solution, three with varying dilutions of the primary culture, and two with the streptococcus in the second culture generation. Six developed markedly increased respiration, five tremors, and four ataxia. The one which remained free from symptoms was injected with a 1:1,000 dilution of the streptococcus in the second culture generation.

Cultures were made in four rabbits that developed symptoms. Those from the brain yielded the green-producing streptococcus in all, those from the blood in one.

The rabbits injected with the primary culture developed similar symptoms in which lateral movements of the head and body, and marked increase in respirations were the predominant features. Both died on the fourth day, and yielded a pure growth of the streptococcus from the brain, whereas the blood was sterile.

SUMMARY OF RESULTS

The ages of the patients ranged from 4½ to 27 years. Three were males and four females. The peculiar symptoms in two followed what appeared to be an influenzal infection; in three they followed undoubted attacks of encephalitis; in one, they developed insidiously from no apparent cause; and in one, coincident with mental strain in a young woman of hysterical tendencies. The duration of the symptoms at the time of study was from one month to one year. In most of the patients, the condition was gradually growing worse. The temperature was normal at the time of the attack in all; hence the likelihood of demonstrating the organism in the blood, or specific antibodies in the serum, was considered too remote to warrant studies along this line. All of the patients had catarrhal pharyngitis. The teeth were normal. The tonsils had been cleanly removed after onset of symptoms in three; one had repeated attacks of tonsillitis, and appendicitis five months before the attack of encephalitis. The streptococcus with which characteristic symptoms were produced was obtained from the nasopharynx in each instance, and from the tonsils also in one.

Of the eighty-three rabbits injected with material containing the streptococcus, sixty-eight (82 per cent.) died. Marked continuous or intermittent hyperpnea was noted in sixty-five, tremor in thirty-seven, ataxia in twenty-five, retraction of the head in eighteen, paralysis in eighteen, spasms of muscles in sixteen, turning of the head in thirteen, nystagmus in ten, rhythmic movements and spasms of abdominal muscles in six each, lethargy in five, and tic-like movements and spasms of the diaghragm in three each. Cultures of the brain and the blood were made in seventy-three, and the characteristic streptococcus was isolated

from the brain in fifty-eight and from the blood in twenty-one. The fifteen in which cultures of the brain were sterile died or were anesthetized long after injection.

Thirteen rabbits were injected intravenously with three of the strains. Localization in the brain, with resulting symptoms, occurred in four. In attempting to simulate closely in animals the condition in the patients, one nostril in each of four rabbits was packed with gauze soaked in the culture. Two remained well, whereas in two localization occurred in the brain, producing characteristic symptoms.

Filtrates of nasopharyngeal washings, or of emulsions of the brains of positive rabbits were made, cultured, and injected intracerebrally into seventeen animals. All remained free from symptoms, and the cultures were sterile.

The factor of dosage was well brought out in an experiment in Case 2. The filtrate of the brain of a positive rabbit was injected into three rabbits. All remained well, were chloroformed twelve days after injection, and were free from lesions. Varying doses of the primary glucose-brain-broth culture were injected into four rabbits. The one receiving 0.1 c.c. of the undiluted culture died in twenty-four hours, with extremely increased respirations; the one receiving 0.1 c.c. of a 1 : 100 dilution in sodium chlorid solution developed markedly increased respiration, varying in intensity, became ataxic, and died five days after injection. Marked leukocytic and round-cell infiltration was found. The one receiving 0.1 c.c. of a 1 : 1,000 dilution, and the one receiving 0.1 c.c. of a 1 : 100,000 dilution remained well, and were free from lesions when chloroformed twelve days later.

The streptococci with which the symptoms were reproduced were culturally very similar. They produced small, dry, non-adherent colonies surrounded by a narrow greenish zone on aerobic blood-agar plates. In glucose-brain broth, they produced a dense, diffusely turbid growth consisting of nonencapsulated, slightly elongated gram-positive diplococci and chains, varying in length. Five of the freshly isolated strains were titrated against my anti-encephalitis and antipoliomyelitis serums, antipneumococcus serums, and normal horse serum. They were agglutinated specifically by the anti-encephalitis and anti-poliomyelitis serums. Details of these and other experiments along similar lines will be reported in another paper.

The virulence on intraperitoneal injection in mice was low. Of seven mice injected with from 0.5 to 1 c.c. of glucose-brain-broth cultures, only two died, without peritonitis, but with localization in the brain. Three guinea pigs were injected intratracheally with 0.5 c.c. of the primary broth culture of one strain for each 100 gm. of weight.

All remained free from symptoms, whereas two injected with the same strain after three rapid animal passages died from hemorrhagic bronchopneumonia.

DESCRIPTION OF SYMPTOMS

The data in the accompanying table do not adequately express the truly remarkable symptoms observed in this series of experiments. The disturbance in respiration was far greater than that in numerous similar experiments in cases of encephalitis, chorea, and spasmodic torticollis. In some instances, there was continuous hyperpnea of extreme grade. Many animals literally breathed with all their might for hours, the rate and amplitude gradually increasing until respiration ceased suddenly and death occurred. In most instances, however, as in

Summary of Results Following Intracerebral Injection of Material Containing the Streptococcus from Respiratory Arrhythmias

Case	Rabbits		Mortality, per Cent.	Spasms of Muscles			Abnormal Movements and Posture						Tremor	Restlessness	Hyperpnea	Convulsions	Paralysis	Lethargy	Animals Cultured	Characteristic Streptococcus In	
	Injected	Died		Diaphragm	Abdominal	Other	Nystagmus	Rhythmic movements of Head	Tic-Like Movements of Head	Ataxia	Turning of Head	Retraction of Head								Brain	Blood
1.....	24	21	87.5	0	1	9	1	3	1	7	4	2	11	2	15	0	4	1	22	16	5
2.....	25	21	84	2	3	3	5	1	1	9	3	12	10	6	23	0	7	1	23	22	8
3.....	8	6	75	0	1	2	0	0	0	1	0	1	1	3	6	2	2	1	8	7	4
4.....	7	4	57	0	1	1	1	0	1	2	0	2	4	1	4	1	1	1	5	2	0
5.....	3	3	100	0	0	0	0	0	0	1	0	0	2	0	3	1	0	0	3	2	0
6.....	9	8	89	0	0	0	2	1	0	1	5	1	4	3	8	1	3	1	8	5	2
7.....	7	5	71	1	0	1	1	1	0	4	1	0	5	0	6	0	1	0	4	4	2
Total..	83	68	82	3	6	16	10	6	3	25	13	18	37	15	65	5	18	5	73	58	21
Normal controls (77)	100	24	23	0	0	2	7	1	3	17	9	2	4	2	10	0	8	0	97	24	7

the patients, extreme alterations in the respiratory rate and rhythm developed. Periods of normal breathing alternated in rapid succession with violent, noisy respirations, and forced expiratory grunts. During periods of normal respiration, the animals usually sat quietly; then from no apparent cause, coincident with the onset of hyperpnea, and paroxysms of sneezing and coughing, they became excited, moved quickly, and developed diverse movements of head and body. In some instances, the head was repeatedly brought under the body; in others, it was moved from side to side in a purposeless fashion, and in still others, it was alternately markedly retracted and flexed. Usually the fore part of the body was elevated, the fore paws often resting on other rabbits; sometimes during paroxysms the fore part of the body was raised so high that the animal lost its balance. The movements of the

head often persisted after the acute respiratory symptoms had subsided, and peculiar behavior was then noted. Sometimes, on slight stimuli, such as slowly bringing the hand or other object over the head without touching the nose, the animals lowered their heads, whereas at other times they refused to do so even when the nose was pushed. Some developed tantrums in which the head was thrown backward and forward in rapid succession; others became cross and fought on slight provocation; still others developed abnormal sexual behavior.

The symptoms in the animals often resembled in particular respects those noted in the patients from whom the strains were isolated. Paroxysms of hyperpnea, alternating with more normal respiration, were a striking feature in animals inoculated with the streptococcus from each of the patients in which it was a noticeable symptom. Continuous hyperpnea, often of extreme grade, dominated the picture in the animals inoculated with the streptococcus from the patient in whom the symptom was predominant. Jerky respirations, especially during expiration, followed the injection of material from the nasopharynx of the patient with this type of respiration, which was believed to be due to a generalized tic of hysterical origin. Moreover, the movements of the body and the head often simulated those noted in the patients. Thus in the experiments in Case 2, retraction of the head occurred in twelve of twenty-five animals injected, which is in sharp contrast to those of the other cases, particularly Case 1, in which only two of twenty-four animals developed this symptom. Five of nine animals injected in Case 6 developed turning of the head, whereas only one of nine developed retraction of the head. As further striking evidence of extremely specific effects of this streptococcus, the results in a series of cases of spasmodic torticollis should be mentioned. Tic-like movements of the head developed in forty-two of seventy animals injected, whereas in the cases of respiratory arrhythmia, this symptom developed in only three of eighty-three animals. Hyperpnea approximating in type or degree that noted in this study developed in only ten of 106 animals injected in the same way with material from the nasopharynx of seventy-seven normal persons.

GROSS AND MICROSCOPIC LESIONS

The findings at necropsy were usually limited to changes in the central nervous system. In the animals that died early, in from one to five days, marked congestion of the vessels of the pia, slight turbidity of the cerebrospinal fluid, and sharply localized edema and infiltration of the pia on the anterior and upper pole of the medulla were almost constant findings. These lesions were often proportional to the degree of hyperpnea, and were similar to those noted in animals injected with the hiccup strains, except that in the latter they extended lower down

and tended to involve the anterior cervical nerve roots. Hemorrhages and necrosis, or other evidence of trauma at the point of inoculation, and focal hemorrhages in brain and cord rarely occurred. Occasionally punctate hemorrhages in the medulla and cervical cord, and more diffuse hemorrhages in the pia were found. In the animals that lived six days or more, or in those that were anesthetized, gross lesions aside from those in the anterior and upper pole of the medulla were usually absent. In a number of animals that had extreme dyspnea during life, marked atelectasis of the lung was found. Hemorrhagic edema of the lungs was not infrequent in those that died soon after injection.

Smears from the cerebrospinal fluid and from the exudate over the upper pole of the medulla revealed leukocytes and mononuclear cells in varying proportions, the former predominating in the experiments of short duration, the latter in those of longer duration. Gram-positive diplococci, usually in pure culture, even when a mixture of bacteria was injected, were readily demonstrated in smears and cultures of material from the animals that died soon after injection, but as the spinal fluid became clearer and the exudate over the medulla was being absorbed in the experiments of longer duration, the mononuclear cells became predominant, and it was increasingly difficult to find the organism in smears or cultures.

The microscopic lesions in the animals that died early consisted of a variable degree of leukocytic and round-cell infiltration, depending on the duration of the experiment. The lesions were nearly always most marked in the anterior and upper part of the medulla, where a thick layer of leukocytes and mononuclear cells was found on the anterior surface, usually with invasion of the anterior part of the medulla. The pia over the posterior part at the same level, or over the cerebrum and the contiguous structures, often showed little or no infiltration. In the animals that developed symptoms and that died or were chloroformed for examination a longer time after injection, round-cell infiltration surrounding vessels and in basal nuclei was the striking picture, and while not wholly limited to the medulla and pons, was most marked in that region. In some instances, it was found in the floor of the fourth ventricle corresponding to the region of the respiratory center. In the acute lesions, gram-positive diplococci were readily demonstrable, but in the subacute lesions in experiments of longer duration in which the infiltration consisted of mononuclear cells, this was often difficult (Fig. 14), and in animals that died or were anesthetized weeks after inoculation it was sometimes impossible either by cultural methods or direct examination of stained sections. The organism was rarely demonstrable in the normal brain substance remote from lesions, even in animals that succumbed soon after inoculation.

Sections were made in seventy-five animals injected with material from the seven patients. Forty-two of these died within four days after inoculation, and the sections of all revealed a variable degree of leukocytic and round-cell infiltration; in three, perivascular round-cell infiltration, probably of spontaneous origin, was also found. Sections were made in eighteen that lived six days or longer after inoculation. All but one of these showed perivascular round-cell infiltration. Sections were examined in ten that were injected with inert filtrates or spinal fluid; of these, one revealed round-cell infiltration. Three of five injected intravenously revealed characteristic lesions. The four that presumably showed perivascular infiltration of spontaneous origin were from two lots of rabbits only. In none of the controls of the other lots was this condition found.

It was hoped that the precise location of the lesion which caused particular symptoms might be determined by a study of the sections, but the lesions were too widespread to permit this. However, it appears certain that the hyperpnea and certain changes in posture were due in the main to lesions in the medulla in close proximity to the respiratory and vestibular centers.

COMMENTS AND CONCLUSIONS

All but one of the patients (the young woman with peculiar jerky respiration with hysterical background) were undoubted examples of marked respiratory arrhythmia following attacks of encephalitis. Streptococci of low general virulence, much alike in cultural characters in the different cases, but with peculiar neurotropic properties, were consistently isolated. The streptococcus resembled those from encephalitis and epidemic hiccup. The specific neurotropic property was manifested by the tendency to localize and produce lesions chiefly in the anterior part of the medulla when injected intracerebrally into the frontal lobe, when injected subdurally just to the right of the median line far forward over the tip of the frontal lobes, when injected intravenously, and when the nose was packed with gauze soaked in the culture.

The symptoms induced in the animals were characterized by extreme alterations of the respiratory mechanism and of posture, and often simulated in one or more important respects those noted in the patients from whom the strain was isolated. They occurred after inoculation of the freshly isolated strains, after several animal passages, and after many rapidly made subcultures. Symptoms did not develop after inoculation of filtrates. Results such as in these experiments were not obtained with material from the nasopharynx of normal persons, nor from patients with other forms of encephalitis.

The organism was demonstrated in lesions characteristic of encephalitis, but which were located chiefly in the medulla. These facts indicate

strongly that the condition is not a sequel to, but a continuation of the initial encephalitic attack, and is due to lesions produced in the central nervous system by a streptococcus having highly specific localizing power. If this be true, the reason these patients fail to respond to treatment is obvious. Healing of damaged areas in the central nervous system long after they have developed rarely occurs. The presence of this streptococcus in portals of entry long after onset of the disease may in part be responsible for the progressive character of the symptoms. Measures, such as removal of evident foci of infection, the use of antiseptics, and the application of specific methods of treatment in the early stages of the disease, should do much to mitigate the distress of this deplorable affliction.

SEX DEVELOPMENT AND BEHAVIOR IN FEMALE PATIENTS WITH DEMENTIA PRAECOX*

CHARLES E. GIBBS, M.D.
Associate in Internal Medicine, Psychiatric Institute, Wards Island
NEW YORK

Many patients with dementia praecox present a variety of symptoms that are definitely sexual in nature, and various theories have been advanced in an effort to explain dementia praecox as essentially a sexual disorder, either mental or physical. The observations to be presented here are part of a study of the sex factor from the standpoints of biologic psychology and physiology. This work has not been inspired by any particular sex theory. It has seemed better at present, especially from the standpoint of research, to consider the sex factor somewhat separately, with the hope of understanding better the origin and nature of the definite sexual manifestations. The necessity is thereby avoided of requiring the observations to explain the entire psychosis.

No preconception has been accepted as to whether the sexual manifestations themselves are primarily psychic or primarily physiologic in origin and nature. It is being more and more recognized that constitutional and physiologic factors, as well as those of environment and experience, enter into the formation of behavior reactions, attitudes, and habits of doing and thinking. In other words, that variations in the biologic mechanism, as well as variations in the stimulus, play a part in determining the character of the response. Sex gland theories have also been avoided. Development and functional activity of the reproductive organs depend, in part at least, on the adequate function of other glands. There is also increasing clinical and experimental evidence to indicate that adequate nutrition and metabolism are essential for normal reproductive function. Of immediate interest is sterility and degenerative changes in the testes produced by variations and inadequacies of diet.

From the viewpoint of behavior, sexual disturbances have been approached as important symptoms, with the hope of gaining a better understanding of the various factors that have played a part in their production. The three most definite factors considered have been instinct, emotion, and the reproductive function in a physiologic sense. The best source of information is a detailed account of the actual sexual experiences through which the patient has passed, and how she has reacted to them. The more we know of what has actually happened

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the better we can estimate the instinct and desire with which the patient is endowed, the emotion and energy with which this instinct has been activated and driven, and the constitutional and environmental factors that have conditioned the reactions. A knowledge of these early reactions and attitudes should enable us to understand better the sexual manifestations in the psychosis. Much of this information must be secured from the patient.

CASE MATERIAL

The observations presented in this paper are based on five series of cases, comprising 546 women, as follows:

(a) An "institute series" of forty-two women patients studied at the Psychiatric Institute, who were classified as dementia praecox by Dr. George H. Kirby. Certain observations in these cases are shown in Table 6.

(b) An "hospital series" of 161 women patients observed on one of the services for chronic patients in the Manhattan State Hospital, including all on this service classed as dementia praecox.

(c) A series of thirty-seven cases studied at the Institute which were classed as manic-depressive psychoses. Reaction type has been the basis of classification rather than prognosis or outcome. Some of these cases had certain malignant features.

(d) A series of seventy cases observed on one of the services in the Manhattan State Hospital, which had been classed as manic-depressive psychoses. These two series of manic-depressive cases will be referred to separately and only with regard to secondary sexual hair.

(e) A "control series" of 235 nonpsychotic pregnant women observed in the antepartum clinic of the Manhattan Maternity, New York. These were selected as the nearest approach to women with normal reproductive function available. Hair distribution was the only factor studied in these cases.

SEX BEHAVIOR IN WOMEN PATIENTS

Most women who develop dementia praecox have been more or less inadequate in sexual behavior. The degree of this inadequacy seems to be rather closely related to the age at which the psychosis appears. A rough index of this is the relation of marriage to the age of the patient when first admitted to a hospital for mental disease, as shown in Table 1. As compared to the women in the general population, the marriage rate is definitely low. The difference is more marked in the earlier age groups. While this may be explained to some extent by saying that patients with early onset have not married because of the early onset, it should not be assumed that the sexual behavior of all

women who develop dementia praecox is essentially the same up to the time when the psychosis appears. The results of this study indicate what seems to be a rather fundamental and significant difference in the character of the sexual behavior in patients with late onset as compared to those with early onset. Patients with rather late onset are more likely to have lived through a period of fairly adequate or satisfactory sexual life, or satisfactory adjustment or compensation, but often with a failure that has a rather close relation to the onset of the psychosis. Many patients with late onset have been sexually active from puberty.

On the other hand, patients with early onset or with a period of definitely seclusive behavior preceding the psychosis, do not seem to have ever reached a satisfactory form of sexual behavior, adjustment or outlet. In these earlier cases there is more evidence of a mental

TABLE 1.—*Marriage in Relation to Age*

Age on First Admission	Dementia Praecox						General Population*	
	Institute Series		Hospital Series		Total			
	Cases	Married	Cases	Married	Cases	Married,† per Cent.	Age	Married,† per Cent.
15-19	9	0	21	0	30	0.0	15-19	5.7
20-24	11	0	38	7	49	14.2	20-24	40.2
25-29	9	3	35	17	44	45.4	25-34	72.3
30-34	4	1	34	18	38	50.0		
35-39	5	3	21	14	26	65.0	35-44	84.5
40-44	4	4	12	8	16	75.0		

* New York state. 1910.
† Widowed and divorced included.

struggle, or of a marked inhibition of function. It is the nature of this difficulty in which we are most interested, and in regard to which opinions differ. There is little question but that these early sexual difficulties are the basis of the sexual behavior and ideas expressed in the psychosis.

SEX INSTINCT

There is considerable evidence that the disturbance in sexual life which so many patients with dementia praecox present, both before and during the psychosis, is not due to lack of sexual desire, disposition, or inclination. Many patients with later onset seem to have had more inclination at puberty, and for some time afterward, than they could socialize. A history of illicit sexual relations was secured in eleven of the thirty-three patients in the institute series who were over 19 years of age when first admitted, a proportion of one in each three patients. There were several others in whom it seemed probable. In the hospital

series, in which no particular effort had been made to determine this point, there was a history of illicit relations in nineteen of 161 patients, or 11 per cent. Ten of these had a total of sixteen illegitimate children, one for each ten patients.

The relation of illicit intercourse to age on first admission is shown in Table 2. A history of illicit intercourse was more frequent in patients with later onset. In most of these patients relations had been started at puberty and had been continued. In the institute series, illicit relations had begun at puberty in seven, and at 21 in another. One of these eight had her first admission at 24, after several years of active sexual irregularity, another at 28, and the other six were over 30. Some had married in a rather incidental way. It is in certain of these later cases that onset of the psychosis is rather closely associated with sexual failure. The ideas expressed are of a defensive nature against the failure.

TABLE 2.—*Illicit Sexual Relations in Dementia Praecox*

Age	Institute Series				Hospital Series			
	Number of Cases	Illicit Relations	Illicit, Later Married	Total Married	Number of Cases	Illicit Relations	Illicit, Later Married	Total Married
15-19	9	0	0	0	21	2	0	0
20-24	11	3	0	0	38	2	0	7
25-29	9	1	1	2	35	4	3	17
30-34	4	2	1	1	34	2	1	18
35-39	5	3	3	3	21	6	3	14
40-44	4	2	2	4	12	3	1	8
Total	42	11	7	10	161	19	8	64

CASE 30 (Institute Series).—The age of this patient on admission was 32. She began having illicit relations at 17 and married two years later, when pregnant. She was not forced into the marriage and married life had been happy. Two or three years before admission she first noticed that her sexual desire had decreased considerably. One year before admission menstruation became irregular and she began to think her husband was cold toward her, and that he was associating with other women. She now says that in some strange way her sexual power has been stolen from her.

In many patients with early onset, and those who have been seclusive, we are told by members of the family that the patient never cared for social affairs or the opposite sex, that they had only girl friends. When we can gain the confidence of the patient, however, we can often get evidence of sexual inclination, evidence that they are responsive to sexual stimuli and sexual situations. They have had love affairs of which the family was ignorant, or they had built up fantastic affairs, and possibly made a trousseau on very slight encouragement from some member of the opposite sex. The episodes which often mark

the onset of the psychosis frequently seem to take the form of a desperate effort at sexual activity. In a few such cases relations are accomplished. There were three such cases in the institute series. In others the behavior and ideas indicate the motive. They stay out at night and walk the streets. They think men follow them and speak to them. One patient, after a failure to be married, took a room in a hotel and said a man telephoned that he would visit her.

In the psychosis the younger patients often show quite clearly their erotic inclinations. It is interesting that erotic ideas are more evident in earlier cases in which actual experience has been most limited. Nearly all of the early cases in the institute series expressed such ideas and inclination, as is shown by the observations recorded in Table 6. Some of these patients have rather childish ideas as to how reproduction occurs. This seems to be due more to a lack of experience and knowledge than to a lack of instinct or inclination.

That a lack of sex instinct is not essential to the types of personality which so often precede dementia praecox is indicated also by the frequency of these types in prostitutes. Treadway and Weldon,[1] pupils of Hoch and Kirby, found that one-fourth of 206 prostitutes had either the seclusive or the superficial, silly type of personality. (Twenty per cent. were of the egoistic-epileptic type, and twelve per cent. were of the emotional type.)

Males who develop dementia praecox have been even more inadequate in their sexual behavior than females,[2] but a lack of inclination or desire does not seem to be the essential reason. Many cases in males have been found to present various behavior characteristics which are quite similar to those recorded here for females.

EMOTION

In certain cases, the previous sexual experiences had been accompanied by an emotional reaction which seemed to be abnormal in intensity or in character. When the patient had had a love affair, whether real and reciprocated, or one-sided, or fantastic, it had usually been accompanied by considerable emotion and was quite desperate on her part. The emotion was out of proportion to the behavior. In some such cases the loss of her sweetheart, or a failure to accomplish a satisfactory sexual life, had produced a definite reaction, or even precipitated the psychosis. Discussion of previous love affairs often elicited definite evidence of emotion, or blocking.

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1. Treadway, W. L., and Weldon, L. O.: "Psychiatric Studies of Delinquents." Public Health Reports **35**:1195, 1247 and 1575, 1920.

2. Gibbs, C. E.: Sex Development and Behavior in Male Patients with Dementia Praecox, Arch. Neurol. & Psychiat. **9**:73 (Jan.) 1923.

Case 27 (Institute Series).—The age on admision was 25 years and 8 months. The mother had been seclusive, and at about the menopause "became insane, excitable and would see things." The patient had been a quiet child; stayed in the house, and was not much interested in play. She learned to dance at 16. Her sister stated that she was secretive about sexual matters, that after a quarrel with her sweetheart she had worried, neglected her personal appearance, was occasionally self absorbed and inactive, and cried easily. Later she developed some antagonism toward this sister who had been going out with boys, and was jealous of her. Later she struck her sister impulsively, and would then cry and be sorry. She became profane to her family. About eighteen months before admission she began talking about a man across the street, saying that he was watching her, and she pulled down the shades. Later, she became silly and covered her head to avoid being looked at. The onset was gradual and progressive.

Soon after admission the following history was secured from the patient. Before she was 19 years of age she had had no love affairs. She had gone to shows with two girl friends, and Ida was her best friend. "She is now married, she was a home girl like I was. I used to think the world of her. Then I met a fellow and did not bother with her any more." She denied having slept with this girl friend or ever having kissed her. At 19, a boy whom she had known for a long time began to pay attention to her. Before this she thought he had watched her when she went out of the house to get groceries and when she went to work. He worked in the neighborhood of her home. He watched her to see what kind of a girl she was. He never talked to her until she met him at 19. He came to see her and took her out to shows. The affair continued for several months. She enjoyed his kisses. She never took him into her home and they did not become engaged. He had another sweetheart at the same time, who was a different type of girl. He went to France and wrote to her, but she did not answer. He is married now and has children. She has not seen him since. At this point the patient cried freely and became restless. After he went away she devoted her attention to her brother, who was also in France, and wrote to him. She never met any other fellows after that. She then cried again, and said she would like to get married and have children.

There was a love fantasy in her psychosis: "I do not go out now because I have my mind on this new fellow; he is supposed to be my sweetheart; I did not meet him; I know him; he is a millionaire; he works near my house; I never spoke to him; I claim he is my sweetheart; (here she laughed freely); "It is to be; he will elope with me; I certainly do like men; when I am asleep I dream of this man hugging and kissing me. I would like to get married; I am getting old; I came here with the intention of getting married; it is not silly." At the staff conference she spoke of her millionaire, became flushed, laughed in an exaggerated, silly way, and had tears in her eyes. "Every night when I go to bed my sweetheart tells me that I am here too long, he might marry another girl." When it was mentioned that she had had a love affair at 19, she showed a strong reaction and quickly left the room.

When examined it was found that she had the masculine type of pubic hair and several hairs on the right breast.

The case was classified: Dementia praecox, hebephrenic type.

In a few of the earlier cases, the reaction to the approaches of the opposite sex has taken the form of fear. This was clearly shown

in Cases 7 and 17. Such cases showed, however, some evidence of instinctive desire.

CASE 7 (Institute Series).—K. R., on admission aged 19, was said to have been bashful and shy in the company of boys, but to have had girl friends. Menstruation began at 15, was irregular, and she did not menstruate for several months after admission. At 16 she became irritable, frequently asked to go to shows, and wanted fine clothes. The psychosis developed gradually. Soon after admission she related an incident in which a boy approached her on the street near her home and asked her to go to the picture show. She was nervous and thought of calling a policeman, but went with the boy. On the way home she had a queer thought that he was going to ruin her or do something to her. She thought she would drop dead in the street. She said: "When it comes to dancing with a boy, I cannot. If a girl would introduce me to a boy I would not know what to do or say. In the presence of boys I am no good at all, I can't face a boy." She talked much of wanting to be married: "I am a beautiful girl, I want to work and have beautiful clothes and get married and have children." She heard the voice of a nice lady who has a beautiful daughter who will take her out and "show me to whom I can get married; she can tell me what to do." She heard the voice of a boy speaking to her at night, telling her that he loves her, will marry her and that she will have fine clothes and a good time; "I picture him in my heart." The nice lady whose voice she heard refers to a woman who lived with the family when the patient was a child, who was kind to her, and who probably suggested some of the ideas expressed in the psychosis.

On physical examination the patient showed incomplete development and would be classed among the cases of polyglandular disorder (Table 6).

The case was classified: Dementia praecox, hebephrenic type.

Although a patient may have been bashful or apparently indifferent in the presence of the opposite sex, it should not be concluded that such behavior is due to a lack of emotion. Such cases as the above indicate that the associated emotion may be intense, and possibly abnormal in character. Dunlap has emphasized that the avoidance of the opposite sex by the adolescent boy or girl is as much a sexual reaction as the more aggressive and active behavior of others. "The violence of his desires and other emotions is responsible for the incoordination" of these reactions.[3] In our patients this form of reaction seems to be more frequent, more marked, and more persistent than in the normal adolescent. In such cases the sexual behavior has apparently been conditioned abnormally, or even inhibited, by emotion.

HOMOSEXUAL BEHAVIOR

A history of active homosexual behavior beginning at puberty was secured in two cases in the institute series. One of these later found greater satisfaction from heterosexual relations and had had illicit

3. Dunlap, Knight: The Elements of Scientific Psychology. St. Louis: C. V. Mosby Co., 1922, p. 222.

relations for several years before marriage. The ideas expressed in the psychosis referred to her husband and to the girls with whom she had homosexual relations. The other case illustrates several of the subjects discussed in this paper.

Case 17 (Institute Series).—This patient was first admitted to a hospital for mental disease at the age of 20. She was active and lively as a child, and a leader in games. As she grew up some mental deficiency became evident, and she was peculiar. Her sisters avoided her and did not want her to go with them. At 16 she learned to dance and swim, and went to dance halls and shows. She met two boys and went to dances with them, but she reacted to this in a peculiar way. She said "It was upsetting me too much, it made me nervous." At about 18 she met another boy who took her to a dance. She said: "As we started home he kissed me, and was rough, and tried to put his hand on my breast. It frightened me, and I ran. I got excited and my girl friend took me home. I like boys, but until I get the right kind I don't like the roughness or the dirty talk. Just a little kiss and no roughness is all right. If a boy takes you out you have to let him do as he pleases. Until I know my mind is exactly right on a boy, until I like him and he knows me, then I would begin to go with him and get married. I think it would be nice to be engaged. Then I would let him kiss me and it would be nice. If he does kiss me and acts rough, I am nervous, I am *afraid* of him. I have felt that way every time a boy has kissed me. I like girls better, my mind is just right for them. They talk sensible. I am not used to boys yet." Further questioning brought out the statement that at 15 another girl had taught her to masturbate. This was followed by homosexual practices which occurred twice weekly for several years, and in which the patient assumed the masculine rôle. Physical examination revealed a masculine type of pubic hair, several hairs on each breast, and hair on the face.

Sometime before admission this patient seems to have developed an attachment for a dentist. This was followed by an acute paranoid episode with a trend referring to the dentist and his wife. She said that he follows her, makes proposals to her and has slept with her, that she was married to him and has had a baby. The child was taken away by a woman who called herself his wife. When asked if she likes him, she blushed and smiled.

It is well known that individuals who display a sexual interest in others of their own sex frequently have some physical characteristics of the opposite sex. They are a sexual mixture, both in personality and physical makeup. The homosexual component may modify their behavior without being sufficiently pronounced to prevent reproduction. It is of interest to note that animals that behave bisexually have been produced by the implantation of ovary into the testicle.[4]

Some evidence of the presence of a homosexual component of a biologic nature in women who develop dementia praecox is the frequency with which the secondary sexual hair shows an inclination to develop in the masculine direction.

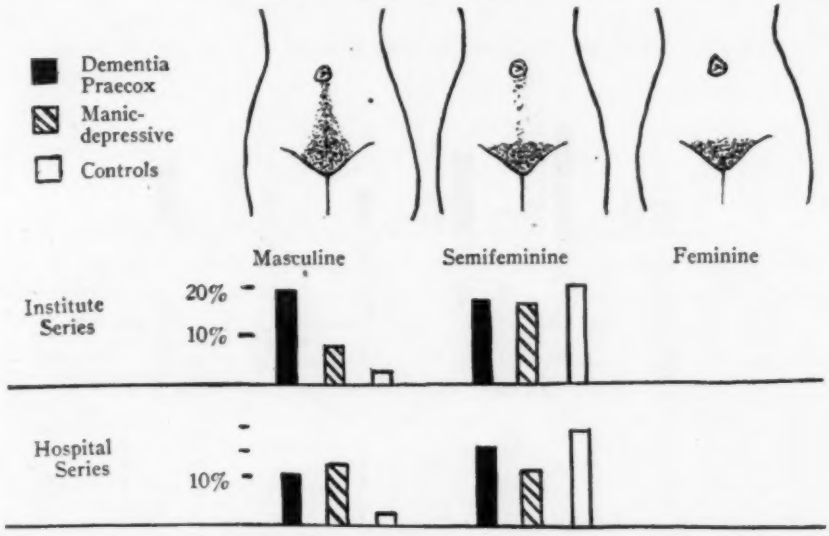
4. Sand, Knud: J. Physiology **53**:257 (Dec.) 1919; Experiments on the Endocrinology of the Sexual Glands, Endocrinol. **7**:273, 1923.

MASCULINE TYPE OF PUBIC HAIR

As indicated in Table 3 the pubic hair was classified as masculine only when it extended to the umbilicus in the typical triangular arrangement without a horizontal limitation. It was classified as semifeminine when there was a feminine distribution with the addition of a few hairs or a narrow strip of hair along the midline.

Definite masculine public hair occurred four times more frequently in the 310 psychotic patients than in the 235 nonpsychotic pregnant

TABLE 3.—*Types of Pubic Hair*



	Number of Cases	Masculine		Semifeminine		Feminine	
		Cases	per Cent.	Cases	per Cent.	Cases	per Cent.
Institute Series:							
Dementia praecox...	42	8	19.0	7	16.6	27	64.3
Manic-depressive.....	37	3	8.1	6	16.2	28	75.6
Hospital Series:							
Dementia praecox...	161	17	10.5	26	16.1	118	73.3
Manic-depressive.....	70	9	12.8	8	11.4	53	75.7
Controls.....	235	7	2.9	46	19.5	182	77.4

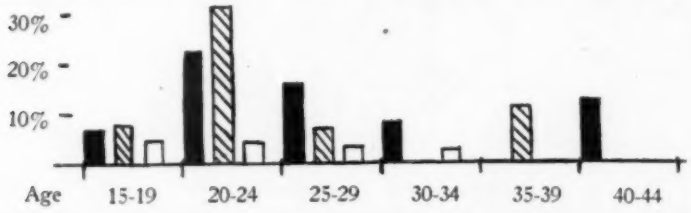
controls. The semifeminine type occurred with almost equal frequency in the two groups. In Table 4 the results are arranged according to age on first admission for the psychotic patients and age when examined for the controls. The findings in each case in the institute series of dementia praecox cases are recorded in Table 6.

Masculine pubic hair occurred in one of every five patients with dementia praecox admitted between the ages of 20 and 29, which was over five times more frequent than in normal controls, and three times more frequent than in patients admitted at other ages. In the institute

series, seven of the eight patients with masculine pubic hair were in this age group.

In the 15-19 age group it was found in only four of fifty-six psychotic patients. These four were over 19 at the time the examination was made. This is in striking contrast to the maximum incidence in the 20-24 age group. This difference is probably due to incomplete or delayed sexual maturity in the younger patients. Several of the dementia praecox patients admitted before the age of 20 were immature and childish in appearance, and showed considerable evidence of disturbed growth and metabolism involving endocrine function (Table 6).

TABLE 4.—*Masculine Type of Hair in Relation to Age on Admission*



Age	Dementia Praecox			Manic-Depressive			Controls		
	No. of Cases	Masculine		No. of Cases	Masculine		No. of Cases	Masculine	
		Cases	Per Cent.		Cases	Per Cent.		Cases	Per Cent.
15-19	30	2*	6.6	26	2*	7.6	23	1	4.3
20-24	49	11	22.4	22	7	31.3	73	3	4.1
25-29	44	7	15.9	29	2	6.9	66	2	3.0
30-34	38	3	7.9	15	0	0.0	47	1	2.1
35-39	26	0	0.0	9	1	11.1	22	0	0.0
40-44	16	2	12.5	6	0	0.0	4	0	0.0
Total	203	25	12.3	107	12	11.2	235	7	2.9

* Over 19 when examined.

In those admitted between the ages of 20 and 29 development had apparently progressed farther, but in a rather mixed way, and masculine secondary sex hair had appeared. Other evidence of endocrine involvment was less pronounced. Those admitted after 30 showed still better development and masculine hair was much less frequent. The presence of an abnormal sexual factor of a biologic nature was indicated, however, by the frequent occurrence of mammary hair even in late admissions.

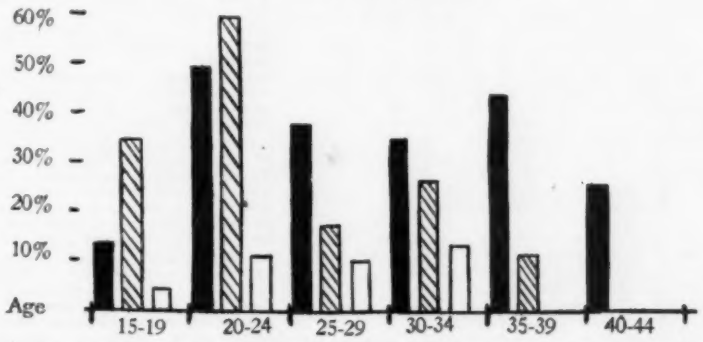
MAMMARY HAIR

Some hair around the nipples and over the sternum is characteristic of men and rare in women. To eliminate any error due to personal opinion, every patient and control was classed as having mammary hair who showed a minimum number of three well developed hairs around one or both nipples. By this standard, mammary hair was

present in 35.6 per cent of 203 women with dementia praecox, and in only 8.9 per cent. of the 235 controls. A complete ring of hair around the nipple is quite frequent in women with dementia praecox, but this amount was not found in any of the controls. As shown graphically in Table 5, the maximum incidence was in the 20-24 age group, in which it occurred in practically 50 per cent of the patients. It showed a high frequency in all age groups after 20, and occurred in only a few patients admitted and examined before 20.

The evidence indicates conclusively that the masculine pubic and mammary hair appeared just after puberty, in both the normal and psychotic women.

TABLE 5.—*Mammary Hair*



Age	Dementia Praecox			Manic-Depressive			Controls		
	No. of Cases	Mammary Hair		No. of Cases	Mammary Hair		No. of Cases	Mammary Hair	
		Cases	Per Cent.		Cases	Per Cent.		Cases	Per Cent.
15-19.....	30	4	13.3	26	9	34.6	23	1	4.3
20-24.....	49	24	48.9	22	12	50.0	73	8	10.9
25-29.....	44	16	37.2	29	5	17.2	66	6	9.9
30-34.....	38	13	34.2	15	4	26.6	47	6	12.7
35-39.....	26	11	42.3	9	1	11.1	22	0	0.0
40-44.....	16	4	25.0	6	0	0.0	4	0	0.0
Total.....	203	72	35.6	107	32	29.8	235	21	8.9

MASCULINE HAIR IN PATIENTS WITH MANIC-DEPRESSIVE PSYCHOSES

Masculine pubic and mammary hair occurred almost as frequently in cases classified as manic-depressive psychoses as in those included in dementia praecox. A review of these cases with masculine hair revealed, however, that many of them had been quite similar to the dementia praecox patients in their sexual behavior and the sexual features of the psychosis, that nearly all of them had displayed mixed or malignant features, and that several of those in series (d) of our material could now be classed as dementia praecox because of the malignant symptoms and the course which the psychosis had taken. In such cases the malig-

TABLE 6.—*Dementia Praecox, Institute Series*

Case No.	Age on First Admission	Pubic Hair			Mammary Hair	Married or Single	Children	Illicit Relations	Notes
		Masculine	Semi-feminine	Feminine					
1	15	..	..	+*	..	S.	..	..	Sex development of girl of 8 or 10. Childish appearance. Has menstruated three times in three years. Thyroid enlarged. Basal metabolic rate, —17 per cent.; —23 per cent. She was "tricked and taken" by movie actors who wanted to make a bad girl of her
2	15	..	..	+	..	S.	..	..	Sex development incomplete. Thyroid enlarged. "If I want to go out with the fellows I guess I can. I had forty-five fellows at my house the night before I came here. I will have all the men I want"
3	16	..	..	+*	..	S.	..	..	Sex development incomplete. Small stature. Childish appearance. A doctor examined her "for immoral purposes"
4	18	..	..	+	..	S.	..	..	Small breasts, autoerotic, disgust in reference to genitalia, disgusted with women because of their sexual characteristics, odors, menstruation
5	18	..	..	+	..	S.	..	..	Hyperthyroidism. Marked fluctuations in body weight. Three remissions
6	18	..	..	+	..	S.	..	..	Thyroid slightly enlarged. Said she was a movie actress and very good looking. A boy put his hand on her shoulder. She fell to the ground and was afraid he would assault her
7	19	..	..	+	..	S.	..	..	Incomplete development. Childish appearance. Amenorrhea Polyglandular type. Thyroid enlarged. Basal metabolic rate, —21 per cent. (For sex behavior and ideas see text.) Fear
8	19	..	..	+	..	S.	..	..	Menses at 14. Irregular. Seclusive personality developed at 14. Was self-conscious in presence of boys. "I noticed that I was not conscious of the opposite sex when I was happy. If I knew I could love I would feel well"
9	17	..	..	+	..	S.	..	..	Restless and erotic. "I talked to a fellow in a picture show and my animal spirits got the best of me." Thinks the hospital may be a "fast house," and that our language is suggestive. Coquettish
10	20	+	..	..	..	S.	..	?	Denies any interest in boys
11	21	..	..	+	Yes	S.	..	..	Small stature. Childish appearance
12	23	..	+	..	Yes	S.	..	Yes	Some hair on face. Relations at onset of psychosis. Said she wanted to be ruined
13	23	..	..	+	..	S.	..	..	
14	23	+	..	..	Yes	S.	..	..	Onset followed marriage of lover to another girl
15	24	..	..	+	..	S.	2	Yes	Illicit relations from puberty, promiscuous (Group II)
16	24	+	..	..	..	S.	..	..	
17	20	+	..	..	Yes	S.	..	..	Hair on face. Active homosexuality. For history see text
18	22	..	+	..	Yes	S.	..	?	Erotic. Productions suggest a sexual experience. Coquettish. Said that any man can do as he wants with her
19	21	..	..	+	Yes	S.	..	Yes	Relations at onset of psychosis
20	20	+	..	..	Yes	S.	..	..	Took a room in hotel and said a man wanted to visit her
21	26	+	..	..	..	S.	..	..	Made a trousseau. Love fantasy. Hyperthyroidism at 17; operation
22	26	..	+	..	Yes	S.	..	..	
23	26	..	..	+	Yes	S.	..	..	Onset precipitated by failure to be married
24	27	..	..	+	..	S.	..	?	Allowed her lover to have relations so he would marry her. Thinks he is now a doctor in the hospital and will write to her

* Deficient in amount.

TABLE 6.—*Dementia Praecox, Institute Series—Continued*

Case No.	Age on First Admission	Pubic Hair			Mammary Hair	Married or Single	Children	Illicit Relations	Notes
		Masculine	Semi-feminine	Feminine					
25	29	..	+	..	Yes	S.	..	..	
26	29	..	+	..	..	M.	..	..	Accuses husband of going with other women and wanted to be rid of her. Is called a bad woman, and is followed by bad women (Group II)
27	25	+	..	..	Yes	S.	..	..	For history see text
28	25	..	..	+	..	M.	1	..	Hair on face
29	28	..	..	+	..	M.	..	Yes	Venereal infection. A doctor lanced something. After that relations were not pleasant. Trend against the doctor (Group II)
30	32	..	..	+	..	M.	2	Yes	For history see text
31	32	..	..	+	Yes	S.	..	Yes	Relations at onset of psychosis
32	34	..	+	..	Yes	S.	..	..	Childish face
33	34	..	..	+	Yes	S.	..	..	Refused to marry. Religious trend
34	36	..	+	..	Yes	M.	1	Yes	Actively homosexual from 12. Illicit heterosexual relations from 19. Married at 32. Hair on face (Group II)
35	39	..	..	+	Yes	M.	2	Yes	Illicit relations from 17. Married at 31. Sex failure. Trend against husband (Group II)
36	39	..	..	+	Yes	S.	..	..	"I like men but they do not understand me." Homosexual references to other women patients and nurses (Group II?)
37	37	..	..	+	..	M.	1	Yes	Illicit relations from puberty. One stillbirth. Married at 35 (Group II)
38	39	..	..	+	Yes	S.	..	..	When asked about relations with woman against whom she has trend, says, "I will not discuss it. Things have happened to my sexual organs. I will not blame her." Homosexual references to other patients. They test her virtue. Also has religious trend and ideas about a priest who was her confessor. Very well adjusted until 31 (Group II)
39	40	..	..	+	..	M.	8	Yes	Illicit relations from 21. Married at 22 (Group II)
40	40	+	..	..	..	M.	..	..	Loss of heterosexual desire five years ago (Group II)
41	42	..	..	+	Yes	M.	1	..	Two stillbirths; five miscarriages (Group II)
42	42	..	..	+	..	M.	?	Yes	Illicit relations from puberty (Group II)

nant features and possibility of a malignant course were usually recognized when the case was classified soon after admission of the patient. Further observations will be necessary, therefore, to determine the occurrence of masculine hair in patients with typical recurrent benign manic-depressive attacks.

CORRELATION AND COMMENT

The observations here reported indicate that in women who develop dementia praecox, definite differences occur in the sexual behavior manifestations and disturbances, both before and during the psychosis, and that these differences have a rather close relation to the age at which the psychosis appears. The cases may be divided roughly into two groups. The first group is characterized by definitely inadequate sexual

behavior and early onset, while the second group is characterized by relatively adequate sexual behavior and late onset.

The first group includes nearly all cases admitted before the age of 30, and a few admitted later. These patients have never been able to accomplish and maintain an adequate and satisfactory form of sexual behavior, although they show considerable evidence of an instinctive inclination or desire to do so, even in cases with the psychosis appearing at puberty. Difficulty in transforming their desire into normal behavior seems to be characteristic of the patients in this group. Although they may have been seclusive, some efforts have usually been made. In some cases a rather desperate attempt at adult sexual behavior in the form of marriage or illicit relations has been closely associated with the onset of the psychosis. In a few such cases illicit relations have occurred in the episode just preceding admission. The efforts at sexual behavior have frequently been associated with an excessive or disproportionate degree of emotion. A few patients have reacted to the approach of the opposite sex with marked fear.

After the psychosis develops the sexual manifestations and ideas expressed continue to refer to desire and its accomplishment. The instinctive desire for normal heterosexual life is frequently fulfilled in dreams, hallucinations, and love fantasies. Previous sexual experiences and difficulties reappear in the mental content. A fairly complete and satisfactory explanation of the definitely sexual ideas expressed is afforded by the previous sexual behavior history.

The second group includes most of the cases admitted after the age of 30, and only a few admitted earlier. These patients have lived through a period of active sexual life or of satisfactory compensation. Illicit heterosexual relations beginning at puberty occurred in over half the cases. What seems to have been a failure in sexual function occurred in certain cases, and in the psychosis the ideas expressed were of a defensive character against this failure. In other cases the failure and ideas were much less definitely sexual.

To a certain extent the physical findings can be correlated with the behavior. The more inadequate the behavior had been, the more evidence there seemed to be of disturbed physical development and reproductive function. Many of the patients with inadequate behavior and early onset, especially those admitted before the age of 20, showed incomplete development of the physical characteristics of sex, and other evidence of disturbed endocrine function. In those admitted after 20, secondary sexual hair of masculine distribution occurred with great frequency, and was often marked in degree.

The patients with a period of sexual activity and later onset showed less disturbance of physical development and were more mature and feminine in appearance. Masculine hair was not so prominent, although

it occurred more frequently than in controls. Reproductive function in these patients seemed to be only relatively adequate.

Such a correlation is further suggested by the rather close relation between secondary sexual hair and sexual activity, as shown by analysis of the institute cases in Table 6. Four of the twenty patients admitted between 20 and 29 had had a period of sexual activity. None of the four showed masculine pubic or mammary hair, while only three of the other thirteen failed to show either masculine pubic or mammary hair. One of these three was childish in development and appearance. And again, while illicit relations occurred in ten of thirty-two patients admitted after the age of 19, and masculine pubic hair occurred in eight, none of those having illicit relations had masculine pubic hair. One patient with masculine pubic hair had been seclusive, but married secretly and said that she was surprised at herself. She lost her desire for relations five years before admission, but in close relation to the appearance of psychotic symptoms. Another patient had hair on breasts and face, and semifeminine pubic hair, but she also gave a history of active homosexual behavior. In the hospital series, also, very few patients with the more marked development of masculine hair gave a history of relations with the opposite sex.

With regard to masculine secondary hair, the following factors seem worth considering in relation to each other:

1. Masculine hair appears just after puberty, between the ages of 20 and 29, in both psychotic patients and normal controls.

2. It occurs with maximum frequency in patients first admitted at this age, and five times more frequently than in controls.

3. It has a close relation to sexual behavior.

4. The maximum number of first admissions occurs in this age period, or a little later.

Masculine hair is interpreted to be merely the surface manifestation of a more profound and widespread biologic disturbance which influences behavior, and which is not confined to the ovaries. Such an interpretation is supported by the rather frequent occurrence of other evidence of endocrine disturbance in patients with the psychosis appearing in close relation to puberty,[5] or after a period of psychopathic behavior beginning at puberty. Previous observations have shown that in certain cases a change in personality occurred at puberty in close association with disturbances of growth and metabolism.[6]

5. Gibbs, C. E.: Disturbances of Growth and Metabolism in Early Cases of Dementia Praecox. The New York State Hosp. Quart. **8**:361 (May) 1923.

6. Gibbs, C. E.: Relation of Puberty to Behavior and Personality in Patients with Dementia Praecox, Am. J. Psychiat. **3**:121 (July) 1923.

The above clinical differentiation is not interpreted to indicate that the underlying pathologic process is essentially different in the two groups, especially in the end results. These clinical differences seem to represent different phases or degrees of compensation of the same functional disturbance. They show a certain semblance to the clinical course followed by certain functional disturbances of endocrine glands, especially of the thyroid and pituitary. Inadequacies of function are often followed by disturbances which have the appearance of overcompensation or overactivity, but in which there may be actually an inadequacy of function.[7] Such disturbances frequently are followed by failure of function, as in the end phases of acromegaly and exophthalmic goiter. Such a conception does not detract, of course, from the etiologic significance of emotional situations in certain cases, any more than the fact that changes occurring in the thyroid in exophthalmic goiter eliminate emotional strain as a precipitating etiologic factor.

7. Plummer, H. S.: Results of Administering Iodin to Patients with Exophthalmic Goiter, J. A. M. A. **80**:1955 (June 30) 1923.

Clinical and Occasional Notes

HEADACHE AND VERTIGO IN URICACIDEMIA*

REPORT OF TWO CASES WITHOUT CLINICAL SIGNS OF NEPHRITIS OR GOUT

WILLIAM H. HOLMES, M.D., CHICAGO

The severe headaches of nephritis and gout, when not the result of vascular disease, are generally regarded as manifestations of intoxication, which usually is indicated by retention of one or more nitrogen compounds. The effect of this form of endogenous intoxication is widespread and consequently disturbances in the function of the central nervous system rarely exist as isolated symptoms. In nephritis there are other clinical signs of renal disease, such as hypertension, cardiac hypertrophy, visual changes, eczema, gastro-intestinal disturbance or changes in the composition of the urine, while in gout any of these findings may be associated with the presence of tophi and arthritic changes. Despite a steadily increasing fund of knowledge of the metabolic changes in these two diseases, the toxin or toxins responsible for the great variety of symptoms remain unknown. Although we are ignorant of their structure, number, and very largely of their mode of action we cannot therefore deny their existence, nor can we assume that they never give rise to clinical symptoms except in association with the diseases mentioned. That such an assumption is unjustifiable is apparently shown by the two cases herewith reported.

In neither case was there a history of a previous attack nor definite clinical signs of existing renal disease or gout, although both cases showed retention of uric acid as high as is ordinarily found in either of these diseases.

At one time, the view that uricacidemia is a reliable index of renal impairment was widely held. At the present time there is no general agreement that it constitutes indisputable evidence of such impairment. In nephritis there is usually not only retention of uric acid, but also retention of urea, creatinin and other nitrogen compounds. Feinblatt (*Archives of Internal Medicine* **31**:758 [May] 1923) is unwilling to consider uricacidemia as evidence of renal disease unless accompanied by retention of other nitrogen bodies. Out of 1,500 routine blood analyses, he reported forty-seven patients who exhibited uricacidemia without concurrent retention of urea or creatinin; and in thirty of these there were none of the signs of renal disease. The forty-seven cases were classified under thirty-five clinical diagnoses not including gout. It is perhaps only natural that the discovery of abnormal amounts of urea, uric acid and other nitrogen bodies in the blood of nephritics should have given rise to the belief that these substances are capable of causing toxic symptoms. Existing knowledge is in conflict with such a view. It does not seem preposterous, however, to assume that if urea or uric acid is retained either in combination or singly,

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* Read before the Chicago Neurological Society, Nov. 15, 1923.

* From the Department of Internal Medicine, Northwestern University Medical School.

* For the blood analyses reported I am indebted to Miss Melanie Schilling, B.S., Physiological Chemist, Wesley Memorial Hospital.

other compounds which have a toxic action may also be retained. Measurement of the degree of retention of urea and uric acid may then be used as an index of the amount of retention of the substances which are yet to be isolated. A step in this direction has recently been taken by Jackson (*Journal of Biologic Chemistry* **57**:121 [Aug.] 1923), who has shown that human blood contains measurable amounts of purin compounds, the principal representative of the group being adenin nucleotid. However, in reporting my cases it is not my purpose to attempt an explanation of the reason for retention nor to speculate on the means by which symptoms such as headache and vertigo are produced, but rather to establish the fact that such symptoms may be observed in patients who present uricacidemia without other signs of renal disease which ordinarily serve to direct attention to the cause of intoxication.

Prior to the appearance of the article of Folin and Denis (*Archives of Internal Medicine* **16**:33 [July] 1915) and that of Myers, Fine and Lough (*Archives of Internal Medicine* **17**:570 [April] 1916), determination of the uric acid content of human blood was neither an accurate nor a common clinical procedure. Since 1916, medical literature abounds in references to headache, migraine, uricacidemia, nephritis and gout. In many of these articles the occurrence of headache and vertigo in nephritis and gout is emphasized, but the occurrence of these symptoms in non-nephritic uricacidemia is not stressed. Isaacs (*Archives of Internal Medicine* **31**:289 [Feb.] 1923) reported a case of polycythemia vera, which, among other things, presented a blood uric acid of 6.9 mg. on one occasion and 8.59 mg. on another without other signs of nephritis. In his discussion of the case he remarks, "It is interesting to note that a persistent headache was relieved fairly quickly following the taking of phenylcinchoninic acid, 0.5 gm., three times a day." Higley and Upham (*Archives of Internal Medicine* **26**:367 [Sept.] 1920) reported twenty-five cases of uric acid retention due to varying causes. Headache was a prominent symptom in twenty cases. Williams (*Archives of Internal Medicine* **27**:748 [June] 1921) reported a group of thirty-five patients with arterial hypertension and with only slight clinical evidence of nephritis. In thirteen of the members of the group, headache was the prominent symptom.

REPORT OF CASES

CASE 1.—Miss. O. E., a student nurse, aged 21 years, was admitted to the hospital as a patient because of vertigo June 1, 1923. There had been two prior admissions because of headache. Her early history is of interest only because of numerous minor illnesses of an infectious type. Furuncles occurred several years in succession. There was gastro-intestinal disturbance at the age of 3 years. The only serious illnesses were diphtheria at the age of 7, and measles which is said to have occurred at the ages of 13, 16 and 17 years. The possibility of there having been nephritis because of these infections naturally exists, but there is no history of such a condition. The headache began in 1919 following the third attack of measles. She stated, "From 1919 to 1923, or up to the time I was put in your care, I used to have headache continually, more so if I would read or bend over. I could notice it more when I would make a bed or when I got excited. During the hot summer months I would have headache every day but I never was dizzy or nauseated until I was taken sick four weeks ago." At the time of her first admission because of headache she described the pain as general in distribution, dull in character, very severe, and constantly present day and night over a period of weeks. It was not relieved by sleep, catharsis, diet, or the ordinary analgesic drugs.

The only other subjective symptom was a feeling of depression. After a few days in bed on a restricted diet the headache gradually abated and she was able to resume her nursing duties. The cause of the headache was not determined although it was felt that it was the result of an intoxication of unknown origin.

A few weeks later she was admitted a second time because of headache, and on this occasion the pain was of such severity that the possibility of brain tumor was seriously considered. Aside from spasticity of the colon the results of physical examination were entirely negative. Blood counts, Wassermann tests and urine analyses, were negative. The basal metabolic rate was plus three. The nonprotein nirtogen of the blood was 42 mg. per 100 c.c. Determination of the blood uric acid was not made. The significance of the nonprotein nitrogen figure was not appreciated because I had previously seen even higher figures as a result of water deprivation. The eyes were examined by an oculist (Dr. Brown Pusey) with negative results. The nose, throat and ears were examined by a laryngologist (Dr. Younger) also with negative results. Anteroposterior views of the skull and spine showed no evidence of disease. All functions of the central nervous system were normal from the objective standpoint. A diagnosis of toxic headache was made but the source of intoxication remained undiscovered. It was thought that the spasticity of the colon with its associated constipation might be responsible and this view was strengthened by the effects of free catharsis following which the headache disappeared.

Relief from pain was of short duration. A few days later while at work in the hospital wards she complained of headache which gradually increased in severity during the two weeks after her discharge as a patient. For the relief of this headache she took a tablet containing phenacetin, caffein and acetyl salicylic acid. About 2:30 a. m., she awoke feeling dizzy and nauseated. On getting out of bed she swayed but did not fall. She then vomited several times. On returning to bed she was annoyed by bilateral tinnitus. The following morning she felt well enough to report for duty and therefore did not seek medical advice. She had headache all that day and at bedtime took another headache tablet. About 2:30 a. m., there was a repetition of the vertigo, vomiting and tinnitus. She was then admitted to the hospital as a patient for the third time.

At the time of examination, about seven hours after the onset of vertigo, she appeared to be sleepy or semistuporous and totally disinterested in her condition and surroundings. On being asked if she was admitted because of headache, she answered, "No, I'm dizzy." Speech was thick and similar to that of a person intoxicated by alcohol. She denied headache, her only complaint being extreme vertigo produced by the slightest movement of the head and associated with tinnitus. Objects seemed to rotate from left to right. The eyelids were kept half closed. The globes were in constant motion in a horizontal direction with the quick component in the direction of visual effort. On looking upward there was a rotatory nystagmus toward the left. The pupillary size, shape and reactions were normal. The media were clear and the vessels and disks normal. Sensation of the face and all facial movements were normal. The tongue was protruded in the median line without tremor. There was no external evidence of aural disease. Hearing for the spoken voice was about normal. With the tuning fork there appeared to be bilateral decrease to both bone and air conduction.

The finding of decrease in hearing was confirmed by an otologist (Dr. Carl F. Bookwalter). In his opinion the vertigo was not the result of labyrinthine

disease. The tendon reflexes of the upper extremities were difficult to obtain. Those of the lower extremities were brisk and equal. There was no spasticity or clonus. The superficial abdominals were present, brisk and equal. Babinski, Gordon, Oppenheim and Chaddock signs were absent. Rapid pronation and supination of the hands were well performed, considering the patient's condition. The finger to finger and finger to nose tests were normally performed. The rebound phenomenon could not be demonstrated. All movements were slow but performed without trace of incoordination. Pointing tests did not show a constant type of deviation. On certain movements an error of two or more inches might occur which was corrected on the second attempt. Examination by a neurologist (Dr. Ralph C. Hamill) showed no change from the findings recorded above. The possibility of encephalitis lethargica was considered and a spinal puncture was made. The fluid was clear, contained no cells, albumin or globulin in amounts above normal and had a sugar content of 0.083 per cent. The circulatory and pulmonary systems were normal. Aside from spasticity of the colon there was no evidence of disturbed function of the gastro-intestinal tract. The breath was offensive; the body temperature was normal; blood counts were negative. The urine on one examination was normal. On three subsequent examinations a trace of albumin was found and in one specimen an occasional hyaline cast. On the second and third days of illness the vertigo was extreme. On the fourth day a chemical examination of the blood was made. The analysis was as follows:

	Mg. per 100 c.c.
Nonprotein nitrogen	36.80
Creatinin	1.45
Uric acid	5.96

Because of the discrepancy between the nonprotein nitrogen and uric acid values, the uric acid determination was repeated on the fifth day, at which time the blood contained 5.87 mg. per 100 c.c. A phenolsulphonephthalein test showed an excretion of 45 per cent. of the dye in four hours. It was on this day that the urine contained a trace of albumin and an occasional hyaline cast. A diagnosis of uricacidemia was made and treatment for that condition instituted. The treatment consisted of fluids in large quantities, a purin free diet and the administration of one 7½ grain (0.5 gm.) tablet of cinchophen four times daily.

At the end of forty-eight hours of treatment the vertigo, nystagmus and tinnitus had disappeared. She was mentally alert and anxious to return to her duties. A uric acid determination showed 1.96 mg. per 100 c.c. of blood. The uric acid excreted in the urine during the second period of twenty-four hours of cinchophen administration amounted to 3.94 gm.

The patient was kept under observation for eleven days without a return of either headache or vertigo. She was on a low purin diet and fluids were pushed, but no drugs were given. During the following month, while away on a vacation, she had two slight headaches which did not last over an hour. On Aug. 2, 1923, the blood showed:

	Mg. per 100 c.c.
Nonprotein nitrogen	26.80
Creatin	1.31
Uric acid	1.20

The urine was normal.

During the latter part of August, while on duty in the diet kitchen, she complained of moderately severe headache on several successive days. It

was found that she was partaking freely of all foods and that the intake of fluids was low. The headache disappeared as soon as she restricted her diet to foods low in purins and increased the fluid intake. No cinchophen was given. Oct. 4, 1923, the nonprotein nitrogen amounted to 34.3 mg. and uric acid to 1.41 mg. per 100 c.c. of blood.

Nov. 12, 1923, nonprotein nitrogen was 38.9 mg., uric acid 2.24 mg., and adenin nucleotid nitrogen 4.59 mg. per 100 c.c. of blood.

CASE 2.—R. J. H., a white man, aged 33 years, was admitted to the service of Dr. C. B. Younger who referred the case for medical examination. The patient complained of headache in the frontal and occipital regions and also of a vertex sensation, described sometimes as a feeling of pressure, and sometimes as a feeling of emptiness. The headaches began in the occipital region about five years before. The frontal headache began about three years before admission, coincident with an acute infection of the upper respiratory tract. The vertex distress is the most recent development and has been of paramount importance only since the relief of pain in the other locations. During the acute respiratory infection the frontal headache, which was pretty well localized to the right side of the head, became almost unbearably severe. At the height of the infection it was suddenly relieved with the discharge into the pharynx of yellow mucopus.

The patient had been subject to recurrences of frontal headache which invariably had been relieved by local treatment directed toward securing better drainage of the nasal sinuses. Neither the occipital nor the vertex headache had been benefited by this form of treatment. Clinical and roentgen-ray examination established the diagnosis of chronic infection of the right ethmoid, frontal and maxillary sinuses, but because of the history it was felt that an additional cause or causes for headache existed. His general attitude suggested that at least part of his trouble was psychogenic in origin.

As in Case 1, examination showed a spastic colon as the only demonstrable disturbance in the alimentary tract. The results of physical examination were otherwise negative. On each of two examinations the urine was entirely normal. On a third examination of a single morning specimen it had a specific gravity of 1.035 and a single hyaline cast was found. The results of all other routine laboratory tests were negative. There was no clinical evidence of nephritis, diabetes or other disease which might cause endogenous intoxication. Chemical examination of the blood disclosed uricacidemia. Nonprotein nitrogen was 51.8 and uric acid 5.83 mg. per 100 c.c. of blood. The treatment outlined under Case 1 was instituted. Blood examination seventy-two hours later showed that the nonprotein nitrogen had risen slightly to 57.1 mg., while the uric acid had fallen to 1.2 mg. per 100 c.c. of blood. An examination of the blood Sept. 8, 1923, three months after discharge, since which he had been on a restricted diet without medication, showed: nonprotein nitrogen, 46.90; creatinin, 1.16, and uric acid, 2.24 mg. per 100 c.c.

Operation on the sinuses of the right side gave complete relief from the frontal headache. The occipital headache also disappeared and has not returned, but the sensation in the vertex has continued.

CONCLUSIONS

1. Uricacedemia may occur without other signs of renal disease.

2. The intoxication implied by the retention of uric acid may be responsible for the production of headache and vertigo.

3. These symptoms may be of such severity as to suggest organic disease of the brain.

4. The symptoms can be controlled by appropriate treatment.

30 North Michigan Avenue.

DISCUSSION

MELANIE SCHILLING (Wesley Memorial Hospital): The method used in our laboratory is that of Folin and Denis, in which we remove the proteins from whole blood, and then precipitate the uric acid with silver lactate. From this precipitate the uric acid is set free by dissolving in dilute acid. With the uric acid in solution, and free from other compounds which might interfere, the characteristic blue color, (a phosphotungstic acid complex) with the Folin and Denis reagent is directly proportional to the quantity of uric acid present; the amount of uric acid is determined by matching the color obtained against a standard. This is the method commonly used in clinical laboratories, and when properly carried out is specific for uric acid. In our records of uric acid determinations were several high ones; in only one case had the patient complained of headache. This case had been discharged from the hospital with a diagnosis of neurosis. The others were all either gout or nephritis.

DR. RALPH C. HAMILL: I saw the first case and was frankly puzzled as to whether there was an encephalitis or not. There was a vertical nystagmus. It seemed difficult to say that there was not some disturbance in the pons. As I recall it, we had difficulty in obtaining the deep reflexes, even in the legs. They were reduced in such a way as to cause suspicion in my mind of the presence of disease in the pons resulting in increased reflex activity. When uric acid was demonstrated, and the headaches and the nystagmus disappeared so quickly, it became difficult to say there was an encephalitis.

DR. H. I. DAVIS: Were other symptoms of hysteria present at that time?

DR. HAMILL: The organic nature of the nystagmus was perfectly obvious, and the condition of the patient certainly was not that of a functional disorder at all.

News and Comment

MENTAL HYGIENE*

During the past fiscal year studies of mental hygiene have been conducted by the Public Health Service under the direction of Surg. W. L. Treadway, who was assigned to this duty Oct. 1, 1922. Through the courtesy of Prof. M. J. Rosenau, of the department of preventive medicine and hygiene, Harvard University Medical School, office space was provided at Harvard.

The demand for scientific information regarding means for the controlling and lessening of mental disease is urgent. In 1880 there were 40,942 persons in the United States under care in public institutions because of mental disease; in 1920 the number had increased to 232,680. The rate increase was from 81.6 per 100,000 in 1880 to 220 per 100,000 in 1920, thus almost six times as many people were under care in public institutions in 1920 and the rate per 100,000 of the population had nearly trebled.

In approaching a program for studies in mental health, the service has confined itself during the fiscal year to those activities which have a bearing upon the problem of mental health conservation. A study of foreign immigration seemed to offer the most desirable method of approach, and a large amount of scattered material has been assembled for publication dealing with the subject of mental health and immigration. This manuscript embraces an interpretation of the concept of mental hygiene and a study of the migrations of people with reference to asocial behavior and mental disease. It also embraces certain preliminary observations on the relationship of types of mental disease to racial stocks and the relative frequency of such disorders, among foreign born, native born of foreign parentage, and native born of native parentage living in the United States. The preparation of this publication included a study of the evolution of immigration laws, an historical résumé of 100 years of immigration to the United States, observations on the medico-legal aspects of mentally disordered immigrants, and recommendations respecting methods for the better exclusion of mentally disordered persons as well as those who are potentially so inclined.

In addition to the above, certain field studies were inaugurated with respect to the problem of asocial behavior and mental disease in foreign-born persons and native-born persons of foreign parentage. The latter studies embrace a social inquiry into the relationship of these problems to mental health.

Observations made upon ethnic groups living in the United States are sufficiently important to deserve mention and are as follows:

1. Senile and cerebral arterial changes productive of mental diseases are more prone to develop in Teutonic and Celtic stocks. Mixed stock in America also ranks high in this respect.

2. Syphilitic brain disease occurs in a higher ratio among the Indo-Eranic, Sinitic, Negritic, Lettic, Finnic, and Chaldaic stocks, whereas the same disease occurs in a lower ratio among the Anglo-American stock.

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*From the Annual Report of the Surgeon General, U. S. Public Health Service, 1923.

3. The Malayic stock is prone to develop mental diseases incident to traumatism.

4. The Celtic are more prone to develop intoxication psychoses than any other stock. The Irish rank first in disorders due to alcohol, while the Slavonic stock is also high in this respect. The Hellenic, Indo-Eranic, and Chaldaic show the lowest ratio of intoxication disorders.

5. Those malignant mental disorders that are associated with faulty mental adjustment occur much more frequently among those peoples comprising the "new immigration." The Tartaric and Hellenic stocks rank highest for this class of disease.

6. Benign mental diseases occur more frequently among Malayic stocks, Anglo-American, Chaldaic, and Sinitic, in the order named. They occur less frequently in the Tartaric, Indo-Eranic, and Celtic stocks.

7. The Anglo-American, Tartaric, and American Indian rank highest for those disorders due to abnormal personal make-up. The Sinitic and Malayic are low.

8. The greatest difficulties are encountered in classifying mental diseases among those peoples in American institutions who are least able to speak the English language.

OFFICERS OF THE NATIONAL COMMITTEE FOR MENTAL HYGIENE

At the annual meeting of the Board of Directors on December 28, 1923, Dr. Frankwood E. Williams was reelected medical director of the National Committee for Mental Hygiene, and the following physicians were elected members of the executive committee: William L. Russell, White Plains, N. Y.; Walter E. Fernald, Waverley, Mass.; Stephen P. Duggan, New York; William A. White, Washington, D. C.; Charles P. Emerson, Indianapolis; C. Floyd Haviland, Albany, N. Y., and Arthur H. Ruggles, Providence, R. I.; also Mr. Matthew C. Fleming, attorney, New York.

A CORRECTION

The secretary of the Central Neuropsychiatric Association announces that an error was made in reporting the name of the vice president elected at the second annual meeting (THE ARCHIVES **10**:687 [Dec.] 1923). Dr. L. B. Alford of St. Louis was elected to this office.

Abstracts from Current Literature

PROBLEMS OF HEREDITY IN MENTAL DISEASES BASED ON PSYCHIATRIC AND GENEALOGIC INVESTIGATIONS OF TWO FAMILIES. FRANZISKA and EUGEN MINKOWSKI, Schweiz. Arch. f. Neurol. u. Psychiat. **12**:47, 1923.

This work was begun in 1912 under the direction of Professor Bleuler and continued until 1915, when it was interrupted by the war, after which it was again taken up. In 1912, two siblings, Emil and Bertha F., were admitted to the institution at Berghölzli. There was a striking similarity between the two cases. In both there seemed to be a mixture of a schizophrenia and manic-depressive psychosis. The disease progressed intermittently with intervals of several years between the various attacks. The first attack seemed to be clearly catatonic. Later, several features developed that did not fit into the ordinary picture of catatonia, and suggested manic-depressive components. At the end of about thirty years, when each had passed through six or seven attacks, a schizophrenic dementia was apparent. The question arose whether cases of mixed psychoses in relatives might not be determined by heredity. This explanation was by no means new and was already suggested by Magnan (1880): "Mania, melancholia, and chronic delirium in the father, epilepsy in the mother, and vice versa, may exercise their action directly on the offspring and simultaneously determine two neuroses resembling the preceding ones, existing coincidentally and without loss of the attributes of either."

In the writers' cases it was found that a schizophrenic type of psychosis was present on the father's side, and that the mother was an epileptic. The investigation was carefully conducted. Not only were the known psychopathic relatives investigated, but members of the families who were supposedly well were visited; and local authorities, friends, and neighbors were consulted. Evidence could be obtained as far back as the great-grandfathers. It was found that the old Mr. F., who lived from 1757 to 1836, was insane, while Mr. B., the great-grandfather on the mother's side, who lived from 1761 to 1835, had epilepsy. No evidence of a manic-depressive psychosis could be discovered.

The problem of determining the existence of a mixed psychosis became obviously great and was gradually replaced by the investigation of all descendants of these two great-grandfathers. It was also necessary to become more or less oriented with reference to individuals who had married into the family. The tree of family F. encompassed 577 persons, of whom 396 were direct descendants of the great-grandfather, while 181 individuals entered the family through marriage. The corresponding figures for family B. were 499 persons, of whom 360 were direct descendants. Altogether the investigation included over 1,000 persons of two family trees covering six generations.

In order to determine the intensity and hereditary malignancy, the apparently well descendants were studied with particular care. The psychologic status and the social behavior of each individual were investigated. In order to do this properly, immediate contact with these people was necessary, inasmuch as written reports could not be relied on.

Because of mortality, small families, and many other factors that cannot be evaluated, the Mendelian law cannot be investigated as it applies to mental disturbances. The following figures were obtained in family F.: In the first generation there was one diseased individual; in the second generation there were eight individuals, of whom two were diseased; in the third generation

thirty-eight, with seven diseased; in the fourth generation, ninety-eight with eight diseased; in the fifth generation, 155 with three diseased; in the sixth generation, ninety-four with none diseased. Clearly there was no tendency to a spread of this disease; indeed the number of diseased individuals reduced itself and finally disappeared.

In family B. the relationship was as follows: In the first generation one individual was diseased; in the second generation of five, none were diseased; in the third, there were thirty-five with two diseased; in the fourth, ninety-eight with ten diseased; in the fifth, 156 with twelve diseased; in the sixth, fifty-six with one diseased. It is to be remembered that among the diseased are included individuals who had only one attack of mental disturbance even though they survived and were well for years subsequently. A progressive degeneration of the stock in these families cannot be said to have existed. In family F. four branches were completely well. Of those branches of the family in which diseased members were present, the number was particularly large, so that the proportion of well individuals was relatively high and one could not speak of a progressive degeneration even in these branches of the family. Another factor must be considered, and that was the very high infant mortality, particularly on the epileptic side of the family. For example, in one generation of ten children, nine died; furthermore, they died of convulsions. Infant mortality and sterility modify the prevalence of disease among descendants. On the whole, however, one could not speak of a tendency to spread, or, of progressive degeneration in these two families. The much disputed law of progressive degeneration, or anticipation of Morel, that is, the earlier appearance of the disease in subsequent generations, could not be demonstrated to hold in these families. There was one exception in family F. Here the great-grandfather had senile dementia, the father developed a schizophrenic melancholia at the age of 52 years, whereas three or four children were committed to institutions at the ages of 22 to 25 years. The psychosis appeared to reach the critical point in the fourth generation. The dictum of Mott, 1910, that all hereditary psychoses either disappear or terminate the descendants within three generations is interesting. In the two families, F. and B., when all things were considered, one could speak only of recessive characteristics.

Qualities which are added to the families through marriage, would exercise leveling and regenerative influences. Many other factors, of course, enter into the appearance of a psychosis; for example, alcoholism, tuberculosis, environment, which cannot all be entered into here. The study of the individual who married into the family demonstrated the fact that convergent heredity, as was to be expected, exerts a very great influence. The writers were unable to add anything in regard to the question of alcoholism. While the material was small, no definite relationship between schizophrenia and tuberculosis could be demonstrated. The social environment seemed to play no rôle in the development of schizophrenia, for those branches of family F. which were spared the disease were less well off from a material standpoint. It was often remarked of the wealthier individuals "They are rich but they are sick," and added, "While we are the poorer, we are the more healthy as a result." The wealthy branches of this family tree suffered as much from schizophrenia as did the others.

The question of a mixed psychosis, or of two psychoses running parallel, was considered. Emil F. was seen a number of times in the institution. The manic components became more and more clear; whereas in the first attacks the dissociation, hallucinations, and catatonic manifestations dominated the clinical picture, during the last attacks the episodes were clearly manic. One

thing did not change, however, and that was the behavior of the patient between the attacks. At these times, we had before us a sinister, threatening person who spent days in bed on and off, who had little contact with other members of the family or the neighbors. The superimposition or layering of a manic-depressive psychosis on a schizophrenia suggested itself. As was said before, however, there was no evidence of a convergence of manic-depressive insanity on the one hand and schizophrenia on the other, to explain this peculiar behavior. The father of the patient was a rather sinister individual. He developed a depression at the age of 52 years following the loss of some money. A diagnosis of melancholia was made. He was discharged unimproved. At home he became quite different. Previously he had been a good father, now he no longer cared about the family, remained in bed, took little care of himself, developed hallucinations of hearing, threatened to set fire to the house, and had to be watched until his death three years subsequently. Here too we had to think of a schizophrenic melancholia. Furthermore, Albertina M. had a mild depression at 14 years of age which recurred every year. At the age of 31 she had to be hospitalized because of an attack of mania. This was followed by attacks occurring in rapid succession. For the past fifteen years she was in the hospital continuously with alternating manic and depressive features, later manifesting a certain amount of psychic deterioration. Elizabeth F. was confined several times because of a mild depression without hallucinations or delusions, lasting about two months at a time. At home she was looked on by others as abnormal; she became corpulent, did not work, was untidy, and was shunned by her neighbors, although she visited a great deal. Sophia F., a sister of the preceding patient, was shut-in, dismal, and distinctly asocial; at a relatively late age she was confined to a hospital because of depression.

The writers believe that the above cases have something in common. All have a tincture of manic-depressive psychosis on the one hand and of schizophrenia on the other.

The following conclusions may be drawn: The epilepsy of the mother did not furnish an explanation of the peculiar clinical picture. It is barely possible that this apparent mixture of two psychoses came about through a union of a manic-depressive and a schizophrenic component. However, if this is true, the union was very firm, could not be separated readily, and seemed to be a characteristic type of psychosis for family F. There were of course typical cases of schizophrenia in the family. Bleuler believes that a further seriation of the schizophrenia group is to be expected on the basis of heredity studies; the background must be illuminated.

The characterologic problem in psychiatry has been recognized for a long time. The necessity of studying the prepsychotic and the post-psychotic personality is obvious. The daily activity of family B. was of a quiet, steady, character. Most of these people stayed at home and were farmers. They visited their home towns if they had left them. There were numerous teachers. In family F. the situation was different. The family estate was sold early. In the second generation they all left the place save one son. Various types of occupation were pursued. Members of the family became widely separated; some disappeared in America. The rich and the poor Fs. did not care to hear from each other. The family members were clearly separated from other members of the community by their type. This was not true of family B. Certain

branches of the family, of course, deviated in certain directions. For example, in one branch of F. a nest of abnormal characters was found; they were a suspicious, litiginous, quarrelsome, dishonest lot and were to be avoided. The mother was referred to as "a bad woman," and the father committed suicide as a means of escape from her. In another branch of family F. there was the grandiose trend. They loved style, lost their sense of proportion, exaggerated greatly and made numerous mistakes. The father and the son were horse traders, bragged when business was good and then lost what they had made. The aunt and the niece went about in full dress and would not associate with other people. No one was quite good enough. The aunt finally married a drunken teacher, the niece, a teacher who was a psychopath. These two branches had on the one hand suspiciousness and quarrelsomeness, and on the other hand grandiosity, but both had in common the inability to meet their environment. In this sense we may speak of "schizoidia." This makeup cannot be looked on as a psychosis but as a type of personality, which, in some cases, may lead to useful results, in others, may lead to a full blown schizophrenia. The writers believe that the intensive study of families will bear much fruit that can be obtained in no other manner. It furnishes the only basis for rational social legislative reforms.

WOLTMAN, Rochester, Minn.

MALIGNANT EPITHELIAL THYMOMA, REPORT OF A CASE WITH NECROPSY. NATHAN CHANDLER FOOT and HELEN HARRINGTON, Am. J. Dis. Child. **26**: 164 (Aug.) 1923.

The patient was a colored child 2 years of age. For some time there had been noted difficulty in swallowing, paroxysms of coughing and strangling while attempting to drink, but no pain. Physical examination showed some dyspnea, the child tending to pull constantly at its throat. Other positive physical findings noted were: hypertrophied tonsils; impaired percussion note over the left side of the chest, with most marked impairment at the apex; roughened voice sounds and diminished breath sounds over the left side of the chest; systolic cardiac murmur. The patient had a rise in temperature, on one occasion to 102 F.; unresolved pneumonia was considered as the probable diagnosis. A roentgenogram revealed a marked increase in all diameters of the heart suggesting a congenital enlargement. Successive roentgenograms showed progressing increase in the density of the left chest with signs of fluid. Aspiration was done but the fluid showed no abnormal cells and cultures were sterile. The patient died, about two months after admission, of cardiac failure and pulmonary edema.

At necropsy a nodular tumor was found compressing the left lung to a small mass, invading the lung on this side and also invading, but to a less extent, the right lung. The remainder of the necropsy revealed chronic passive congestion of the liver, spleen and suprarenal capsules, and chronic hyperplasia of the mesenteric lymph nodes. Microscopic examination of the tumor showed cells of the following types: (1) reticuloid, resembling the embryonic thymic reticulum; (2) epithelioid, resembling an adenocarcinoma or a medullary carcinoma, and (3) carinomatoid, resembling a large round cell lymphosarcoma or fibrosarcoma.

In commenting on this case the authors note the difficulty of diagnosis because the distribution of the growth produced in the roentgenogram a shadow indis-

tinguishable from an enlarged heart. The heart showed no anatomic abnormalities and the dyspnea and systolic murmur presented by the patient are traced to compression of the trachea and the aorta by the tumor mass.

VONDERAHE, Cincinnati.

A CONTRIBUTION TO THE STUDY OF NERVOUS PALUDISM. C. PAPASTRATIGAKIS, Rev. neurol. **29**:394 (April) 1922.

By nervous paludism the author means the entire syndrome of clinical nervous symptoms associated with a malarial infection, directly or indirectly involving the liver, kidneys, etc. Nervous paludism may be acute or chronic, febrile or afebrile, but always accompanied by the presence of the parasite in the blood. Nervous paludism usually accompanies the febrile crisis. The principal forms are neuralgic and meningeal. They may be associated or independent. The neuralgic form and especially the vasomotor form give rise to the so-called larval nervous paludism. In such cases the nervous manifestations are essentially transitory or recurrent, and apparently take the place of the febrile crisis, and might be called febrile equivalents. It is not with this aspect of the subject, however, that the author is concerned as others have covered the field well; but it is rather with the nervous manifestations which appear in the course of chronic paludism not generally accompanied by fever. This is the more obscure aspect of the subject, and the one least understood.

The author then gives a brief resumé of his subject under five heads: Meningeal manifestations, cerebral manifestations, medullary manifestations, neuritic manifestations, and the so-called "marsh neuroses," or what might be called the "neuroses of paludism."

1. *Meningeal Manifestations.*—The literature on the subject between 1902 and 1909 dealt only with acute manifestations, such as an acute meningitis or simple meningismus. The author first called attention to the chronic meningeal symptoms in 1921. They are similar to those described by Lepine in the course of "chronic rheumatism." The nervous manifestations are completely afebrile. In some cases paludism seems to have entirely disappeared; but examination of the blood always reveals the presence of the parasite. Clinically the chronic meningeal signs include a positive Kernig sign, active reflexes, a moderately high lymphocytosis of the spinal fluid, and sensory symptoms (radiculitis) of the lower extremities. The upper extremities have never as yet shown any sensory disturbances.

2. *Cerebral Manifestations.*—Disorders of cerebral circulation are the most common. Here are to be considered speech disturbances and disorders of motility, almost always of short duration, and spontaneously curable. Epilepsy may manifest itself, but in this case it is to be distinguished from ordinary epilepsy by the rise in temperature which immediately precedes the epileptic crisis, and by a lymphocytosis of the spinal fluid. Fever and lymphocytosis of the spinal fluid differentiate malaria or palustrial epilepsy from epilepsy following paludism. It is here also that we have to be on the lookout to distinguish or differentiate hemiplegia due to arterial embolism (produced by malaria) as seen in the young, from hemiplegia due to syphilis. Hemiplegia due to malaria is surprisingly frequent in countries where malaria is common.

The author warns the reader not to confuse residuals or sequelae of epidemic encephalitis with cerebral symptoms in cases of paludism, an error made as early as 1851 by Ouradon. He also points out the danger of confusing a true radiculitis with a monoplegia supposedly secondary to malaria in which there is cerebral involvement.

Under the cerebral manifestations the author also speaks of abortive forms, such as pure vertigo, and motor incoordination in certain cases of paludism with cerebral symptoms.

3. *Medullary Manifestations.*—Myelitic symptoms are rare. The author has seen but two cases. There is occasionally a syndrome not unlike that of multiple sclerosis in which there are spasticity, tremors, and nystagmus; but the author has never found the Babinski sign. Certain cases of malaria with cord symptoms, therefore, may exhibit what may be termed a pseudo multiple sclerosis. Another group of cases show urinary syndromes, including vesical paralysis and spasm of the urethra. There may also be nocturnal enuresis, but the author thinks that as a rule such cases usually show some of these symptoms preceding the attack of malaria followed by what seems to be cord involvement.

4. *Neuritic Manifestations.*—Clinical descriptions have been common since the time of Rey (1869). The present article draws attention only to the fact that the clinical symptoms frequently appear at long intervals after the last febrile crisis. Facial paralyses, for example, sometimes develop many months after the fever, accompanied by the presence of the parasite in the blood. Another interesting feature in the history of malarial neuritides is that of the ease with which any nerve whatsoever may be affected, whether it be sensory, motor, or mixed nerve. Cranial, trunk, or peripheral nerves alike are affected. This one peculiarity is rarely met with in the course of other toxic processes. (It should be remembered that malarial neuritides are essentially toxic in character.) When the neuritis is due to malaria, its symptoms are the outstanding ones even when associated with some other toxic agent such as lead in the neuritis of plumbism.

Under malarial neuritis and polyneuritis the writer also notes the fact that vasomotor and trophic disturbances are frequent complications. He cites the case of a patient who, every day at a certain hour, without any accompanying elevation of temperature, had periods of shortness of breath and anxiety followed by an urticaria localizing itself over the chest and abdomen. There was also cyanosis of the hands. The condition lasted over a period of three or four hours. During this period, the plasmodium was found in the blood. These phenomena have led investigators to the belief that the malarial crisis is nothing less than a nervous shock, anaphylactic in character, due to the action on the nervous system of certain heterogeneous albuminoid substances.

Prognosis in malarial neuritides must be guarded. Treatment is symptomatic. Quinin apparently has no effect. Arsenic and electrotherapy may be helpful. For the chill quinin of course is of value.

5. *Malarial Neuroses.*—Some writers, especially those describing the anxiety neuroses, deny any connection between the latter and malaria. Heckel thinks the anxiety features are due to the fact that the patients are usually such as would have anxiety attacks, psychic in character, simply because of their being strangers in a strange land, colonists in a word. Their malaria only accentuates their homesickness. M. Vinchon on the other hand, in his work based on observations made in the psychiatric service of the army of the Orient, has studied the relation between malaria and anxiety hysteria. He believes they are closely associated. From his studies it might be asserted in a general way that there can be no malarial crises without anxiety symptoms; but between simple anxiety and the pure anxiety neurosis there is a breach which every malarial victim does not leap. In brief, an emotionally unstable patient who

contracts malaria is more apt to manifest symptoms that resemble the true anxiety neurosis than is the emotionally stable individual. A typical case is then cited.

The concluding paragraph presents two opposing views as to the pathologic mechanism of the anxiety attacks in malarial victims. One, that of Vinchon, traces the anxiety symptoms to vasomotor disturbances, the result of the action of the plasmodium on the nervous centers.

The author takes an opposing view, and champions the theory of endocrine disturbance, most notably that of the thyroid, particularly hyperthyroidism. He thinks most cases show an enlarged gland, and exophthalmos. The subject demands further study.

JONES, Detroit.

EXPERIMENTAL OBSERVATIONS ON THE ETIOLOGY OF CHOREA. EDWARD C. ROSENOW, Am. J. Dis. Child. **26**:223 (Sept.) 1923.

Rosenow reviews the work of Collins, La Fetra, Camisa, and Quigly in reference to their isolation of cocci from the blood of chorea patients and the work of Poynton and Paine who isolated a diplococcus from the spinal fluid of a patient with rheumatic fever presenting choreiform symptoms. The work of Westphal, Wassermann and Malkoff, and of Richards and others is also reviewed to substantiate the opinion that chorea minor is a streptococcic disease.

Rosenow obtained cultures from the tonsils and nasopharynx in four typical cases of chorea. Characteristic localization followed intravenous and intracerebral inoculations, as well as infection of the teeth in dogs. The organisms were specific in their localizing properties in the brain; this specificity was retained through three successive animal passages but was lost after ordinary aerobic cultivation of the organisms. The clinical symptoms produced in dogs resembled those of chorea in man; the anatomic changes in the central nervous system consisted of inflammatory areas within or adjacent to the motor centers or motor paths of the cerebrum, midbrain and cerebellum. The lesions in the heart valves resembled those found in chorea in man. As controls, animals were inoculated with streptococci from cases of encephalitis, epidemic hiccup and ulcer of the stomach, from throats of normal persons, and from persons suffering with anterior poliomyelitis; in these, localization rarely occurred in the heart valves, joints or muscles, and with the exception of strains from the myoclonic types of encephalitis, the lesions in the central nervous system did not induce symptoms similar to those following injection of strains from chorea. A monovalent serum prepared from an inoculated horse agglutinated all choreic strains but had no such effect on the five control strains of streptococci.

Rosenow suggests, on the basis of his own findings and the reports of others, that chorea is due to a streptococcus having specific neurotropic and immunologic properties and obtainable from the tonsils, nasopharynx and teeth of the affected persons.

VONDERAHE, Cincinnati.

PHOTIC ORIENTATION IN INSECTS WITH SPECIAL REFERENCE TO THE DRONE-FLY, ERISTALIS TENAX AND THE ROBBER-FLY, ERAX RUFIBARBIS. S. O. MAST, J. Exp. Zool. **38**:109 (Aug. 20) 1923.

Experiments were undertaken to ascertain the movements involved in the process of orientation in insects and the relation between these movements and various conditions of illumination. *Eristalis* and *Erax* are photopositive on

the wing as well as on foot. *Eristalis* orients accurately, especially when on foot. *Erax* does not orient very precisely. When laterally illuminated, both turn directly, without trial, to the source of light. In orienting on the wing, they turn up or down as well as to the right or left. With light from two sources, both go toward a point between the sources. The greater the difference in intensity of the light received from the two sources, the nearer the more intense illumination the point is located. In flying specimens this holds with the beams of light in any plane. It indicates that the orienting response depends on the location of the stimulus in the eyes. When the flies are oriented in light from two sources on a horizontal line the two eyes are not equally illuminated. With the front leg on one side removed the flies orient nearly as precisely as normal specimens. If the front and middle legs on one side are removed *Erax* goes fairly directly toward the light for a short distance and then deflects toward the normal side. *Eristalis* walks more freely at first, deflecting toward the normal side, but orienting fairly accurately after a few days. This shows that orientation is not necessarily dependent on balanced action in locomotor appendages of opposite sides. Specimens of *Eristalis* with the front and middle legs on one side removed and either eye covered proceed fairly directly toward the light. If the direction of the light is changed they reorient by turning, showing that the movements of the legs on either side may be controlled by impulses originating in either eye. If the front and middle legs on one side are removed and the eye on the opposite side is covered, illumination of the posterolateral surface of the other eye induces backward movement of the legs on the normal side; illumination of the lateral surface, lateral movements; illumination of the anterior surface, forward movement; and illumination of the anteromedian surface, forward movement toward the median line. This shows that the response depends in part on the location of the stimulus in the eye, and not solely on the magnitude of the stimulus.

If one eye is covered *Erax* tilts toward the normal side. The degree of tilting is greater in strong than in weak light. If the lower portion of one eye is covered and the upper portion of the other is also covered *Erax* leans toward the latter even if this eye receives less light than the other. This indicates that tilting is largely dependent on the illumination of the ventral surface of the eye and is intimately correlated with the location of the stimulus in the eyes. The tilted posture is held for long periods, even after the light that induced it has been removed. When *Erax* is tilted the legs on the blind side are more extended and tend to move faster than those on the normal side. This results in circus movements which seem to have little significance in orientation. If one eye is covered both *Eristalis* and *Erax* turn, in nondirective light, continuously toward the functional eye. In a horizontal beam *Eristalis* with one eye covered deflects toward the functional eye at first, but later it orients fairly accurately. This is probably due to readjustment in the orientation mechanism depending on experience. Orientation is possible with only one functional eye and is consequently not necessarily dependent on a balance in the effect of the light on receptors located on opposite sides. If the stimulus is localized at the posterior edge of the retina with one eye covered, the feet on one side move forward while those on the other move backward, the two front feet deflecting toward the side stimulated, the two hind feet from this side. If it is localized in the lateral portion both front feet move laterally toward the light, as do the middle feet. If it is localized in the central part

of the anterior surface of the eye the feet on both sides move forward and the insect does not turn. If it is localized at the anteromedian edge it turns toward the covered eye. Similar reactions occur in normal specimens if the stimulus is localized in one eye. Stimulation of different regions of the retina in either eye alone sets up in the legs on both sides coordinated reflexes of such a nature that they tend to direct the organism toward the source of stimulation. Orientation is brought about by a series of reflexes. In photic orientation the nature of each series of reflexes depends on the localization of the stimulus in the eye. The elimination of the effect of stimulation in one eye by simultaneous stimulation in the other eye is due to the total absence of any appreciable effect of the stimulating agent on the muscles of the legs. An insect can go fairly directly toward the light without being continuously stimulated and held on its course, because, in the absence of directive stimulation, it tends to take a straight course; and because, if it turns slightly from the oriented position, the locations of the illuminated regions in the retina change, setting up orienting reflexes which bring it back into the oriented position. These facts prove that the tonus hypothesis, or any other that demands balanced action in receptors and locomotor appendages on opposite sides, does not fully account for orientation in insects.

WYMAN, Boston.

THE PATHOLOGY OF NODULAR (ADENOMATOUS?) GOITERS IN PATIENTS WITH AND IN THOSE WITHOUT SYMPTOMS OF HYPERTHYROIDISM. LOUIS B. WILSON, Am. J. M. Sc. **165**:738 (May) 1923.

The author presents the accepted classification of exophthalmic goiter as follows: (1) Early exophthalmic goiter, with moderate increase in basal metabolism and usually moderate exophthalmos. In this condition there is moderate thyroid enlargement. The parenchymal cells show marked hypertrophy and moderate hyperplasia. There is diffuse hyperemia throughout the gland; (2) advanced exophthalmic goiter with high metabolic rate, usually marked exophthalmos and a well marked nervous syndrome. There are usually marked thyroid enlargement, advanced parenchymal cell hypertrophy and hyperplasia, and little if any stored colloid. The gland is diffusely hyperemic. (3) Late exophthalmic goiter with high but sometimes declining metabolic rate, exophthalmos and a well marked nervous syndrome. Pathologically the changes in the gland are similar to those in the earlier stages of exophthalmic goiter but with beginning or well marked storage of colloid. Many follicles containing colloid are lined with flattened parenchymal cells. In some instances newly developed follicles are numerous. Hyperemia is usually materially less than in glands in the previous groups.

After the study of thyroids from about 250 patients, the author feels that a shifting of the grouping to the following is somewhat necessary: (*A*) Patients with enlarged nodular thyroids and symptoms of hyperthyroidism, but without exophthalmos or the nervous manifestations characteristic of exophthalmic goiter, and with basal metabolic rates of 20 or more points above normal; (*B*) patients of approximately the same age with enlarged nodular thyroids, without symptoms of hyperthyroidism and with basal metabolic rates within 10 points of normal.

Group A.—In about 90 per cent. of all thyroids there is evidence of increased activity in the parenchymal cells, associated with some colloid storage. Many

of the glands are: (a) diffuse colloid goiters without evidence of new follicle formation; (b) colloid goiters with no definite follicle formation and no definite capsules, but with some hypertrophic change in the parenchymal cells (adenomatosis); (c) definitely encapsulated areas of new follicle formation with hypertrophic and often hyperplastic parenchymal cells lining follicles which contain little or no stored colloid.

The most advanced parenchymal cell hypertrophy and hyperplasia is found in thyroids of the true exophthalmic goiter series, but in most thyroids in Group *A* there was a marked colloid storage in the follicles, whereas in the true exophthalmic series little or no colloid is found. From the pathologic evidence alone, the author does not feel warranted in concluding that the formation of new follicles is the essential factor in the production of hyperthyroid symptoms, since in almost all glands, even when this is the predominating picture, there are many areas which indicate absorption of colloid by reactivated parenchymal cells.

Group B.—In about 95 per cent. of these thyroids there was little cell hypertrophy and hyperplasia, most of the cells being of adult type and uniformly flattened or atrophied. The intrafollicular colloid in this group stained much more densely than in thyroids of Group *A*. All the patients showed a nodular type of gland.

Because of the work of Boothby and others, Wilson feels it may safely be assumed that in thyroid disturbances the basal metabolic rate is a true index of the degree of hypothyroidism or hyperthyroidism. He suggests that an inviting hypothesis ascribes the symptoms of nonexophthalmic hyperthyroidism to the adsorption of complete thyroxin in previously stored colloid, which is being manufactured more rapidly than in the normal gland but much more slowly than in the thyroid of exophthalmic goiter. This hypothesis receives support from the facts: that the symptoms produced by the administration of thyroxin in large doses to human beings are essentially those of nonexophthalmic hyperthyroidism; that stored colloid does contain thyroxin, and that the histologic picture indicates that colloid is being transferred from the follicles to the circulation.

He feels that we might go a step further and speculate on the probability that true exophthalmic goiter is caused by an incompletely elaborated thyroid secretion, an antecedent of thyroxin, for instance, without the normal quota of atoms of iodine in its molecule. Such an hypothesis would harmonize many of the clinical and pathologic findings. However, an equally alluring hypothesis is that, in true exophthalmic goiter, the primary onset of the disease is in the nervous system, and that the more striking symptom of thyroid hyperfunction is nevertheless a secondary development.

TEMPLE FAY, Philadelphia.

GASTRO-ENTEROSPASM AS A MANIFESTATION OF AUTONOMIC IMBALANCE IN EARLY INFANCY. PARK. J. WHITE, Am. J. Dis. Child. **26**:91 (July) 1923.

White draws a clear distinction between hypertrophic pyloric stenosis, a congenital malformation, and pylorospasm. In those instances in which medical treatment (atropin, lavage, thick cereals as food) fail, the cause is most probably hypertrophic pyloric stenosis. The author notes that in many cases, pylorospasm is associated with diarrhea and that a more proper term would be gastroenterospasm. In order to explain the constipation, which is generally regarded

as a prominent symptom, the author suggests that the stool may be hurried through the small intestine to remain for a long time in the sigmoid and colon. The parasympathetic innervation of the stomach and small intestines is from the bulbar autonomic, while that of the large intestine is from the sacral autonomic, and autonomic activating agents have different effects on varying divisions of this system. The author regards the syndrome, usually referred to as pylorospasm, as due to increased parasympathetic tone probably because of an increased production of cholin. Tetany, protein sensitization, the exudative diathesis and parenteral infection are regarded as having an etiologic relationship. In a group of cases analyzed, the principal manifestations noted were: (1) fretfulness aggravated by feeding, (2) projectile vomiting with diarrhea or constipation and with or without visible intestinal or gastric peristalsis, (3) absence of tumor at the pylorus, and (4) ready response to atropin therapy.

VONDERAHE, Cincinnati.

PATHOLOGIC ANATOMY OF LANDRY'S PARALYSIS. GRÜNEWALD, J. f. Psychol. u. Neurol. **29**:55, 1922.

The writer reviews the numerous works on this much discussed subject which was first defined by Landry and Kussmaul in 1859. Duchenne was probably the first to recognize the probability of poliomyelitis being the underlying disease process in Landry's paralysis, and Schmaus in his critical review of the subject found it impossible to differentiate the two conditions satisfactorily.

Grünewald was unable to draw any conclusions regarding the pathologic anatomy of this disease from the literature as the reported findings differed so markedly. In his own material, he observed definite nerve changes with Wallerian degeneration. The cervical region of the cord showed the major changes, consisting of necrotic foci and hemorrhages. The parenchyma was swollen and, with Nissl's stain, the anterior horn cells, the ganglion cells of Clark's column, of the tractus intermediolateralis and of the paracentral group showed the most marked changes. Perivascular infiltration, especially about the vasocorona, as also some degenerative changes in the lateral and posterior tracts was noted. Most of the changes occurred in the cervical and medullary region, to a less degree in the lumbar and dorsal segments. The cerebrum also showed mild changes as ganglion cell degeneration, glial increase, hyperemia and transudation. Increase in ameboid elements was not pronounced and but few polymorphonuclear leukocytes were present. In view of the early peripheral nerve involvement the possibility that one is dealing with an ascending neuritis must be borne in mind.

The differentiation of Landry's paralysis from myelitis, poliomyelitis and polyneuritis is considered. While, as a rule, the paralysis appears to be the result of an infectious process, an etiologic factor frequently cannot be determined. Grünewald considers the chief changes to be of a degenerative nature affecting especially the lipoid substances. Due to these lipoid changes there exists a marked variation between clinical and pathologic findings. These changes the author considers to be of a toxic nature and constitute a group to which many cases of Landry's paralysis belong.

It is the writer's belief that Landry's paralysis should no longer be considered a clinical entity but that it may be based on various types of processes, as poliomyelitis, myelitis, polyneuritis, even epidemic encephalitis. It is in reality a symptom-complex representing a phase in the disease process. At

times the lack of pathologic findings suggests a toxic process which may become localized either in the bulb, medulla, cord or peripheral nerves, but at no time does the diagnosis of Landry's paralysis indicate a specific etiology or pathologic anatomy.

MOERSCH, Rochester, Minn.

TETANY IN THE ADULT, WITH SPECIAL REFERENCE TO ALKALOSIS AND CALCIUM METABOLISM. WILDER TILESTON and FRANK P. UNDERHILL, Am. J. M. Sc. **165**:625 (May) 1923.

The authors classify tetany as primary when it occurs endemically, as in certain parts of Europe, and secondary when its appearance is noted in certain diseases, especially those involving the gastro-intestinal tract. In three cases presented, the sodium bicarbonate content of the blood was found abnormally high, while the calcium was below normal. They call attention to the work of MacCallum, who showed by ligation of the pylorus and repeated gastric lavage, that removal of the hydrochloric acid produced a condition similar to tetany. with marked increase in the blood bicarbonate and diminution of the chlorids. The administration of sodium chlorid relieved the tetany. In all three cases the carbon dioxid combining power of the blood was increased, but it is pointed out that this does not necessarily mean a change in the hydrogen ion concentration toward the alkaline side, as the increase in bicarbonate can be, and in most cases probably is, compensated and there is no change in the reaction of the blood. The term "alkalosis" should be restricted to cases in which the p_H of the blood is actually increased.

In future work on tetany in the adult, it would seem desirable to determine both the p_H and bicarbonate of the blood, as well as calcium and other elements. It has been found that some forms of tetany occur without change in the calcium concentration. From the work of Loeb, Matthews and others, it appears that the excitability of the neuromuscular mechanism varies directly with the ratio of $Na + K : Ca + Mg$., so that it is theoretically possible for increase of irritability to result from either a decrease of the calcium or an increase of the sodium. In cases complicated by nephritis with acidosis, marked decrease occurs in serum calcium without producing tetany. It is apparent, therefore, that decrease of calcium alone will not cause tetany.

Experimentally, tetany has been produced by simple over-ventilation of the lungs in healthy subjects. The urine shows a rapid fall in titratable acid. The carbon dioxid combining power of the blood falls with increase of the p_H, while the calcium becomes somewhat increased. Explanation is given for the apparent anomaly of an alkolosis associated with sodium bicarbonate, by the supposition that the carbon dioxid is washed out of the blood more rapidly than the alkali can be removed, which leads to a decrease of the ratio $H_2CO_3 : NaHCO_3$.

The authors note that many cases in the literature had an associated diarrhea, usually of pancreatic origin. Their conclusions are that there is still much to be learned as to the pathogenesis and the ultimate cause of this remarkable condition.

TEMPLE FAY, Philadelphia.

REFLEXES OF THE NEW-BORN. FRANCESCO DE ANGELIS, Am. J. Dis. Child. **26**: 211 (Sept.) 1923.

De Angelis studied the reflexes of eighty-eight infants during the first week of life. The children were all healthy and the examinations were made repeat-

edly under varying conditions but never repeated sufficiently often to cause fatigue. The author notes that Babinski, attributing the phenomenon which he described to alteration of the pyramidal tracts, deduced as a corollary of this conception that the phenomenon should be physiologic in the new-born because of the insufficient myelinization at birth. De Angelis, however, is of the opinion that the usual response of the plantar reflex in new-born infants is plantar flexion of the toes; in his cases, 57 per cent. showed flexion and 43 per cent. showed extension although there was much variability and great difficulty at times in deciding the type of response. The abdominal reflex was elicited with difficulty and required testing during sleep or while the child nursed. The cremasteric reflex was present in 92 per cent. of the cases. The corneal and pharyngeal reflexes were present in all cases. The patellar reflex was present in all but 3.5 per cent. of the cases with a general tendency to exaggeration. The pupillary reflexes varied widely; in 62 per cent. the reflex consisted of a series of alterations of the pupil beginning with a contraction on luminous stimulation followed by dilatation. The author in conclusion notes that all reflexes may be present at birth, that when present they are extremely variable, and that therefore only the absence of the reflexes can be of pathognomic importance.

VONDERAHE, Cincinnati.

GENERAL PARALYSIS IN STATE HOSPITALS FOR MENTAL DISEASE. EDITH M. FURBUSH, Ment. Hyg. **7**:565 (July) 1923.

Statistics are always interesting. They are particularly so when they deal with preventable diseases. To obtain a bird's eye view of the physical and mental ravages of general paralysis through the medium of accurate statistics should stimulate prophylactic and therapeutic effort to the utmost.

Included among 16,297 male first admissions to state institutions for the insane, there were 2,474 general paralytics and among 12,702 women there were 553 cases. Adding cases of cerebral syphilis we come to a realization of the fact that one of every six individuals who develop mental disease does so primarily because he has contracted syphilis. The age of greatest incidence is from the beginning of the fourth to the end of the fifth decade of life, and 70 per cent. of all general paralytics first show typical symptoms between the ages of 30 and 50.

It is worthy of note that a larger percentage of men and a smaller percentage of women with high school or college educations succumb to paresis than to all other forms of mental disease combined. Urban centers furnish 84 per cent. of the patients as against 68.2 per cent. of all the other classes of mental disease. There is a higher ratio of alcoholic intemperance than in any other psychosis. Almost 60 per cent. of general paralytics are married, and the condition is twice as common in single men as in single women. The highest rate of occurrence is found among persons employed in domestic and personal service, in actors, authors, editors, reporters, musicians, and music teachers, and the lowest rate among clergymen, draftsmen, physicians, and school teachers. One may question even the small recovery rate of 0.4 per cent.; naturally the death rate is higher than in all other mental disorders, and the majority of the patients die between the ages of 40 and 45. In other psychoses the apex of the death curve is reached after the age of 70. The average hospital residence of the paretic is less than two years. One may readily agree with this conclusion "the prevalence and fatal character of

general paralysis point out the urgent need of more extensive and intensive efforts to check the spread of syphilis and emphasize the importance of applying treatment in the early stages of the disease, so that its later disastrous developments may be prevented." To this may be added the hard won conviction of neuropsychiatrists that the maximum of effort must be directed, not against general paralysis, but against syphilis. In other words, the only individual who is absolutely sure of escaping general paralysis is the individual who has never contracted syphilis.

STRECKER, Philadelphia.

SOME ASPECTS OF NEUROPATHY IN INFANCY. CORNELIA DELANGE, Am. J. Dis. Child. **26**:83 (July) 1923.

The author reports three cases of infants presenting compulsory attitudes. The attitude assumed was a strong backward curve of the head; the muscles were not hypertonic; the position of the head could be altered without resistance, but the child tended to resume the abnormal state, evidently preferring this posture. A necropsy performed in one instance showed nothing abnormal in the central nervous system. In one case in which the respiratory curve was studied, it was found that there was a disturbance of the natural rhythm characterized by periods of apnea and prolonged inspiration. In this case there was no organic brain disease and the gas metabolism and circulation were normal; accordingly, the author concludes that the symptomatology was due to a functional derangement of the cerebral cortex. The author warns against making a diagnosis of a functional condition in infancy, pointing out that the cases described above are unusual, and calls attention to the fact that as a rule a position of opisthotonus is due to organic brain disease.

VONDERAHE, Cincinnati.

THE EFFECT OF CHEMICALS ON LOCOMOTION IN AMEBA. I. REACTIONS TO LOCALIZED STIMULATION. J. GRAHAM EDWARDS, J. Exp. Zool. **38**:1 (Aug. 20) 1923.

Solutions of chemicals were allowed to diffuse over a small portion of the surfaces of amebas by means of capillary pipettes with extremely small apertures. The investigation was designed to determine what reactions result from local changes in the surface of ameba induced by chemicals, with the purpose of revealing something concerning the nature of the local changes at the surface and the probable rôle played by these in ameboid movement. Cultures of *Amoeba proteus* were used for the experiments. The results follow. When acids diffuse against the anterior three-fourths of an ameba, a protuberance, short and blunt if the acid is strong, and finger-like if it is weak, is formed at the point where the acid comes into contact with the surface. The formation of protuberances seems to be conditioned by a liquefaction of the ectoplasm. This is followed by a gelation of the ectoplasm after which it visibly contracts and soon the protuberance disappears. When hydroxid of sodium or potassium is used the response consists in the gradual formation at the point of contact of a broad protuberance when the hydroxid is strong and of a more slender protuberance when it is weak. The protuberances do not as a rule persist. The response is apparently conditioned by a liquefaction of the ectoplasm but without subsequent gelation. Ammonium hydroxid induces an eruptive advance of the ectoplasm toward the source of stimulation followed immediately by

a cessation of streaming and the assumption of a somewhat spherical form. When salts diffuse against the surface of an ameba the response consists usually in a contraction of the ectoplasm at the point stimulated, followed by a bending of the ameba away from the source of stimulation and the formation of one or more pseudopods on the side opposite the stimulated region. The response to salts is in general variable and depends on the composition of the salt, the concentration, and the medium in which the amebas are located when stimulated. Changes in permeability seem to condition this type of response. When alkaloids are applied to amebas the response consists in a slight contraction of the ectoplasm in the region where the reagent is applied, and the formation of a pseudopod on the opposite side. Quinin and cocain induce the formation of protuberances toward the pipette. Some of these persist. Cane sugar causes so many changes in streaming that locomotion is practically stopped. The effect is probably osmotic. Alcohol produces a hyaline blister at the point to which it is applied and then streaming is diverted away from the pipette. Weak solutions of alcohol cause streaming to be diverted away from the pipette, but no blisters are formed. Potassium cyanid applied without neutralization with hydrocyanic acid produces a small protuberance which does not persist. When it is applied after it has been neutralized the ectoplasm contracts at the point where it is applied and streaming is diverted away from the pipette. The leukobase of methylene blue, if applied before it has undergone appreciable oxidation, causes violent contraction over the area to which it is applied. Streaming is stopped momentarily and then is resumed away from the pipette. When it is applied after it has undergone considerable oxidation, there is a slight contraction of the surface and two or more pseudopods arise on either side of the area stimulated and curve toward each other forming a protoplasmic cup. The action seems to be one of gelation only. Hydrogen peroxid induces cessation of streaming, followed almost immediately by locomotion away from the reagent, and within a minute by detachment from the substratum and inactivity. The effect on the ectoplasm is not obvious.

WYMAN, Boston.

A CASE OF COMPLETE DECEREBRATE RIGIDITY IN MAN. F. M. R. WALSHE, Lancet **2**:644 (Sept. 29) 1923.

The case described was one of suprapituitary tumor, which filled the third ventricle. The clinical symptoms began suddenly and developed rapidly, death ensuing in about six weeks in spite of a decompression. During this time there appeared first a left and two weeks later a right hemiplegia, and gradually increasing coma. Analysis of the clinical appearances after the double hemiplegia permitted the recognition of two stages: decerebrate rigidity, and failing reflex activity with tonic fits. The picture corresponds closely with that described by Sherrington and differs markedly from the parkinsonian syndrome of extrapyramidal disease.

In the first of the two stages, the attitude was typical of decerebrate rigidity with the exceptions that the upper limbs maintained a flexion posture, and control of body temperature was retained. To explain the former Walshe suggests, as he has before, the fact that the upper limbs in man are no longer simple locomotor props, but have taken on new and highly complex functions. The second exception is regarded as evidence that the decerebration was not quite complete. In addition to the posture, the patient presented well marked

tonic neck reflexes of Magnus and de Kleijn. Using the extensor plantar reflex as a component of the flexion reflex of the lower limb, it was also possible to demonstrate a marked change in the flexion reflex by change in the position of the head.

During the last five or six days of life, the picture of decerebrate rigidity gave place gradually and progressively to loss of reflex activity and deepening coma. The Magnus and de Kleijn reflexes disappeared and the rigidity waned. During the last week, numerous tonic seizures lasting from fifteen to sixteen seconds occurred, but ceased entirely in the last twenty-four hours. Respiratory and cardiac irregularities accompanied the seizures.

SINGER, Chicago.

PRELIMINARY REPORT ON THE KOTTMAN REACTION IN CHILDREN, WITH A NOTE ON THE TREATMENT OF CHOREA WITH THYROID. JOHN D. LITTLE and LUCY PORTER SUTTON, Am. J. Dis. Child. **26**:179 (Aug.) 1923.

Lyttle and Sutton studied the Kottman reaction in children hoping to discover a means of differentiating between various types of endocrine disturbances in their early stages. The Kottman reaction as performed by the authors consists essentially of noting the rapidity of the color change (reduction of silver nitrate) by serum in the presence of potassium iodid and measured exposure to light. One hundred and six children were tested. Twenty-eight were chosen as controls; of these twenty-one were normal. The authors were unable to obtain satisfactory results in their endocrine cases because of the small number, uncontrolled treatment and other factors. Acceleration was found to be the predominating reaction in a group of cardiac cases. A tendency to acceleration of the reaction was found in cases of chorea; Kottman, and also Peterson, having shown that increased thyroid secretion retarded the reaction, thyroid extract, was tried in a number of these instances with marked relief of the symptoms.

VONDERAHE, Cincinnati.

DIABETES INSIPIDUS: A CASE REPORT FOLLOWING EPIDEMIC ENCEPHALITIS WITH ENORMOUS POLYURIA. GEORGE W. HALL, Am. J. M. Sc. **165**:551 (April) 1923.

The author presents a case in which the symptoms of diplopia, marked drowsiness, pain in the back of the neck and night sweats, with slight bilateral ptosis, suggested the diagnosis of encephalitis. Two years later, the patient complained of intense thirst, ravenous appetite and frequent micturition. The daily urinary output ranged between 5,000 and 30,000 c.c. It was markedly increased by the administration of glucose and an increased sugar tolerance was found. Epinephrin and pituitary extract relieved the condition temporarily. A review of experimental work on the pituitary gland and adjoining structures, apparently points to involvement of the tuber cinereum and the hypothalamus, rather than the posterior lobe, as a cause for polyuria.

Bailey and Bremer have shown recently that polyuria and polydipsia are produced with certainty by a very slight injury to the postinfundibular region of the hypothalamus. A recent editorial in the Journal of the American Medical Association states that, at present, it cannot be concluded that disorder of the pituitary body is in all cases the cause of polyuria. Study of reported cases emphasizes the need for more definite information regarding the precise location of brain centers governing the action of the kidney. Hall cites a case of diabetes insipidus, reported by Herrick, which showed marked reduction of polyuria following lumbar puncture with relief of pressure.

In treating diabetes insipidus, posterior lobe pituitary extract has an immediate but transitory effect. Lumbar puncture in some cases has been of value. But the only nonsurgical treatment that seems to be of permanent value is the restriction of sodium chlorid and nitrogen in the food. In cases of syphilitic encephalitis, specific treatment generally has had little effect on the diabetic syndrome.

TEMPLE FAY, Philadelphia.

EXTENSIVE HEMORRHAGIC EXTRAVASATION FROM THE VENOUS SYSTEM OF GALEN, WITH A CLINICAL SYNDROME. A REPORT OF THREE FATAL CASES WITH TWO NECROPSIES. CHARLES BAGLEY, JR., Arch. Surg. **7**:237 (Sept.) 1923.

Bagley reports three patients with cranial injury who succumbed after showing a similar clinical picture. A very marked rise in temperature, with accompanying rise in pulse and respiration were noted. The patients were stuporous, muscle power was affected to a greater or less degree and increase of deep reflexes was present. The muscular disturbance was chiefly of the spastic type. The pupillary reactions were disturbed. The cerebrospinal fluid was bloody, and there was marked lowering of the intracranial pressure. In two cases that came to necropsy, the structures anatomically related to the vein of Galen and its tributaries were most seriously and definitely damaged. Hemorrhages were observed in the corpus callosum and there were occasional small extravasations throughout the lenticular and caudate nuclei.

He believes that the syndrome presented can be accounted for by the lesion described. Some of the signs, for example, disturbance of muscles, spasticity, weakness and increase of deep reflexes, are fully accounted for by the pathologic findings; while others, hyperpyrexia, unconsciousness, and low intracranial pressure, could, perhaps, better be attributed to lesions of this part of the brain than to those of any other.

This paper is of particular interest to those who deal in neurosurgical problems. The picture described is that attributed loosely to medullary edema. If the disturbance can be shown to be due to a circulatory lesion, limited to the vein of Galen, our conception of the causative factors of medullary edema may have to be changed.

GRANT, Philadelphia.

BIRTH HEMORRHAGE INTO THE SPINAL CORD WITH RESULTANT BLADDER AND KIDNEY COMPLICATIONS. CARL O. KOHLBRY, Am. J. Dis. Child. **26**:242 (Sept.) 1923.

In the case reported here, birth was by breech presentation; delivery was not unusually long although there was difficulty in disengaging the head. The day following birth it was noted that the child's breathing was diaphragmatic; there was some movement of the arms and legs. Spinal puncture performed on the fourth day showed a xanthochromic fluid and numerous red blood cells on microscopic examination. There was no evidence of hemorrhage elsewhere. Later, the child showed a fixed flexion of the forearms, paralysis of the thoracic and abdominal muscles and paralysis of the leg. Paralysis of the bladder developed with resulting bilateral hydro-ureter and hydronephrosis and subsequent infection of the genito-urinary tract. The child died with a terminal bronchopneumonia at the age of 9 months. At necropsy, a completely degenerated cord was found in the lower cervical region.

VONDERAHE, Cincinnati.

RENAL INSUFFICIENCY IN MENTAL DISEASES. RENÉ TARGOWLA and M. BADONNEL, Presse méd. **31**:782 (Sept. 12) 1923.

The figures obtained by urea determinations (i. e., Ambard's constants) are compared with the percentages found in phenolsulphonephthalein (Rowntree and Geraghty) excretion tests. In different diseases the findings were not always parallel, though usually so in dementia paralytica; the urea constant might be raised and the phenolsulphonephthalein excretion normal, or the latter reduced and the urea normal. Renal insufficiency was demonstrated frequently in cases of dementia praecox and regularly in cases of dementia paralytica, less often in confused and melancholic states, rarely in manic states. In dementia paralytica, this renal insufficiency was charged to vasoparalytic lesions of the kidney. In the other psychopathies, in which it was generally associated with signs of hepatic insufficiency, it appeared to vary directly with the clinical condition. Renal insufficiency, then, was not appreciably influenced by diuretics and cardiac tonics, but did improve pari passu with improvement in the mental state, whether the latter was effected by symptomatic treatment or by clearing up spontaneously. When clinical recovery was incomplete, the insufficiency was likely to remain, and may have contributed to the chronicity of the mental symptoms by failure in elimination of toxins. Renal insufficiency, though sometimes lacking, appeared to be part of the symptom-complex of certain dementias and other psychoses. It was important to distinguish between this as a concomitant symptom, and a preexisting nephritis as a determining cause of a given psychosis.

HUDDLESON, New York.

FURTHER COMMUNICATION ON DISSOCIATION OF FACIAL MOVEMENTS. G. H. MONRAD-KROHN, Saertryk av Norsk. Mag. f. Laegevidensk. **84**:715 (Aug.) 1923.

It has long been known that in central facial paralysis there is often a marked dissociation between voluntary and emotional innervation—the latter being less affected than the former. The author points out that in cases of peripheral facial paresis one may once in a while find a faint suggestion of this dissociation, when emotional innervation seems to result in a slightly stronger movement than voluntary innervation. But never does any pronounced dissociation obtain as in central (pyramidal) facial paresis, in which the emotional innervation often remains completely intact. The author has described several cases of this complete dissociation.

The author now relates some further observations which show that in central facial paresis the emotional innervation not only remains intact, but is even distinctly exaggerated on the paretic side. By means of slow motion kinematographic pictures it is also shown, that the emotional movements are also quicker, i. e., accelerated on the side which shows paresis on voluntary movements.

On the other hand he mentions a case of postencephalitic parkinsonian state, in which the emotional innervation of one half of the face showed distinctly more impairment than the voluntary innervation.

PATTEN, Philadelphia.

EXOPHTHALMIC GOITER IN CHILDHOOD WITH SOME UNUSUAL MANIFESTATIONS. HENRY HEIMAN, Am. J. Dis. Child. **26**:216 (Sept.) 1923.

Heiman reports three cases of exophthalmic goiter in children aged 4, 5, and 7 years respectively, all of whom were girls. No hereditary tendencies

to the disease could be established. There was a negative history of syphilis; in the two cases in which a Wassermann reaction was made the result was negative. One patient was operated on; portions of the thyroid studied showed considerable colloid with hyperplasia of the parenchyma. The symptomatology was essentially that of the disease in adults: tachycardia, enlarged thyroid, exophthalmos. There was an elevation of basal metabolism directly proportional to the severity of symptoms and signs. The mentality of the children was above the average. For treatment, the author suggests a period of physical and psychic rest for from six to ten weeks, followed by roentgen-ray therapy if the rest is of no avail. If both these measures fail, thyroidectomy is advised.

VONDERAHE, Cincinnati.

BRAIN ABSCESS, WITH ESPECIAL REFERENCE TO ABSCESS OF THE FRONTAL LOBE. HARRY HYLAND KEER, Arch. Surg. **7**:297 (Sept.) 1923.

Kerr reports his experience with frontal lobe abscess. He feels that, owing to the fact that the abscess is located in a relatively silent area of the brain, diagnosis is difficult. This statement is born out by the fact that only about one half of the reported cases of frontal abscess were correctly diagnosed prior to necropsy. The mortality in these cases is high, owing to the difficulty of diagnosis and the possibility of meningitis following the establishment of drainage. Any case with persistent headache, leukocytosis, retinal changes and a history of infection in or about the frontal sinuses should be explored. To reduce the chance of postoperative meningitis, Kerr believes in two-stage operation, the first stage being directed toward the production of adhesions in the subdural space, about the area through which the drainage tract is to pass. He emphasizes the importance of draining the abscess for a long time, shortening the drain very slowly. Brain abscesses must heal by the formation of scar tissue from within outward. Unless the drain is kept in place until the abscess cavity has been thus entirely obliterated, the possibility of the formation of a residual abscess is great.

GRANT, Philadelphia.

DEMENTIA PRAECOX AND ARSPHENAMIN. MAURICE PAGE, Presse méd. **31**:807 (Sept. 22) 1923.

This is a short report of five cases that were diagnosed clinically as typical dementia praecox and treated with intensive courses of neo-arsphenamin. Symptomatic cures were obtained in four cases, without relapse, over follow-up periods averaging several years. The fifth case showed marked improvement, almost recovery. The most interesting feature was a family history of syphilis in four cases of the series.

HUDDLESON, New York.

THE TREATMENT OF INFANTILE TETANY WITH ULTRAVIOLET RADIATION. LYNNE A. HOAG, Am. J. Dis. Child. **26**:186 (Aug.) 1923.

Hoag studied the effect of ultraviolet radiation on the clinical symptoms and on the calcium concentration of the blood serum in eleven cases of infantile tetany. Ultraviolet rays were applied in amounts approaching the limits of tolerance and unaccompanied by other treatment. The application resulted in a permanent and progressive relief of the clinical symptoms paralleled by the

return of the serum calcium concentration to an essentially normal figure. A return of the serum calcium concentration to 9.5 or 10.0 mg. in 100 c.c. was used to judge the completeness of the cure.

With the mercury vapor lamp at a distance of 50 cm., the average total exposure necessary to cause an increase in serum calcium of 1.0 mg. in 100 c.c. was found to be fifty minutes. An average of fourteen days was required for the calcium to rise from its initial low figure to 9.5 mg. in 100 c.c. of serum.

VONDERAHE, Cincinnati.

Society Transactions

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Regular Meeting, Oct. 18, 1923

F. K. Hallock, M.D., *President, in the Chair*

A CASE OF MYELITIS OF UNUSUAL ETIOLOGY. Dr. J. W. Courtney.

The patient, born in Ireland, aged 47, for twenty-five years a club servant, was referred to me Aug. 17, 1923. The family history is unimportant. The patient was married at 25, denies venereal disease and has not abused alcohol. His health was excellent until October, 1922, when he had an exceptionally severe attack of bleeding piles. For two months the loss of blood at stool was profuse. At the end of that time he noticed numbness of the right great toe followed by a burning sensation in the ankle. This was followed by marked trepidation in the muscles of the right lower extremity. The numbness gradually extended from ankle to knee and from knee to the lower abdomen. About three months later, numbness and trepidation appeared in the left lower extremity. The numbness ultimately reached a level just above the symphysis. At that time great difficulty was experienced in starting the urinary stream, although the urine was passed freely with the stools and the patient could feel the flow. Defecation was difficult, but there was no loss of sensibility in the rectum. There was no fever and the patient was not confined to bed. There has been no pain aside from a "neuralgic feeling" in the knees. For eight weeks prior to my first examination there was dragging of the right leg, and for three weeks the left leg had been spastic. There has been no disturbance in the power of erection; the upper extremities were not affected. The numbness experienced up to the time the left leg became spastic was purely subjective.

Physical Examination.—The patient was fairly well nourished but rather pallid; he had never had much color in his face. Walking without assistance was impossible. The gait was not only spastic and ataxic, but it was further embarrassed by an extraordinarily severe myoclonus which involved practically all the leg muscles. The cranial nerves and upper extremities were normal. The heart area and sounds were normal. The spine was normal in contour and flexibility. With the patient seated, the clonic spasms diminished markedly, but voluntary movement increased them at once. Muscular atrophy was entirely absent. All forms of sensibility were blunted but not lost throughout the legs to the level of the symphysis. The knee and ankle jerks were enormously exaggerated. The slightest upward pressure on the plantar surface of the foot produced a violent and persistent ankle clonus. The Babinski phenomenon could almost be produced through the sole of the shoe. Weakness of the lower extremities was marked.

Comment.—In arriving at an etiologic solution of the case I could not escape the conviction that the appearance of the primary numbness of the right great toe synchronously with the severe hemorrhoidal attack was not a mere coincidence. The free anastomosis of the hemorrhoidal system with the spinal

venous system suggested strongly that one of two things had taken place: either an upward extension of hemorrhoidal thrombi or an infection through these veins

With this idea in mind, I referred the patient to Dr. MacAusland and urged immediate exploration of the rectum. This was made by Dr. Ralph Jackson, who is present and will, I hope, tell us what he found and what he subsequently did in an operative way. The trepidation practically ceased before the patient left the hospital after Dr. Jackson's operation. Since his discharge from the hospital, his locomotive powers have improved to such an extent that he now makes his way about the house without artificial aid, and gets along the street with the aid of a cane alone. Spasticity is still distinctly present, more marked in the left leg than in the right. Ankle clonus and the Babinski sign still persist, but the patient has been gaining constantly in flesh and strength. I am inclined to believe, in last analysis, that the cord changes, which must have found their highest level opposite the fourth sacral roots, were nutritional and that they were brought about by blocking of the venous outlet at that point.

DISCUSSION

DR. RALPH W. JACKSON: I found a definite internal hemorrhoidal condition, more marked on the left side of the anus, and an indurated column running upward toward the seminal vesicle on the right side of the ampulla. This latter was not tender or discernibly fluctuant; it felt like scar tissue, and was suggestive of a sinus, though I could find no opening. We decided on operation, and I first incised the indurated column, which collapsed somewhat, and may have contained a few drops of pus, but, if so, it was not discerned on account of the blood from the hemorrhoids. I then did a radical operation for the hemorrhoids, enucleating them in a manner that is as different from an ordinary hemorrhoid operation as a tonsillectomy is from a tonsillotomy. The hemorrhoids were not excessively large nor more definitely infected than in the ordinary case.

The rectum and anus as possible foci of infection are sadly overlooked. I have seen a number of cases of arthritic conditions which have been benefited or cured by adequate drainage of obscure fistulous tracts therein, and the possibility of absorption of infection from infected hemorrhoids is undeniable. I have had no experience with distant consequences arising, as Dr. Courtney has worked it out, from venous thromboses originating in the anorectal field, but anatomically there would seem to be no reason to deny the possibility of such conclusions; and they would seem to be justified in this case in view of the results of operation, which were so prompt and astonishing that I thought at first they must be psychic, but they are continuing and the patient is getting well.

DR. COURTNEY: I will say a word about another case seen some years ago. The patient was a strongly built Swede. Some weeks before I saw him he was unloading a hen coop from a dray. The coop slipped and produced an abrasion of the skin of the patient's right anterior chest wall. Within a week a small abscess formed at the site of the abrasion. The physician to whom the man went paid no special attention to this abscess. Within a relatively short time the patient noticed an increasing embarrassment in locomotion. With this there were later associated anesthesia and vesical sphincter disturbance. When I saw the man he had all the signs of a transverse myelitis. My opinion was that the pus had travelled back through the lymphatics to the cord. Dr. Ayer's necropsy findings confirmed my diagnosis.

DR. J. B. AYER. The case referred to was one of frank epidural abscess, which extended to the back from an original focus in the breast. The spinal cord at the level of compression was liquefied, due as we thought to the combined effect of pressure and toxic substances. Another case of epidural abscess was seen with Dr. Taylor, and although the pus was drained within forty-eight hours of the initial symptoms of myelitis, degeneration evidently took place, as the patient became paraplegic.

We can hardly correlate these two cases of epidural abscess with Dr. Courtney's case. Such a mechanism as he works out in this case seems possible in view of what we know of ascending toxic neuritis.

DR. COURTNEY: Just a word in answer to Dr. Ayer, I see only analogy not identity in the two cases. I merely instanced the second case to show from what apparently innocent causes and through what roundabout routes the cord may be involved.

A CASE OF AMYOTROPHIC LATERAL SCLEROSIS WITH SIGNS OF PAGET'S DISEASE. DR. HENRY R. VIETS.

So far as I have been able to ascertain, no case of this character has been reported in the literature. The patient, aged 53 years, was seen in August, 1923, complaining of weakness of voice, arms, and legs. He gave up work as a railroad executive three years before, and had been spending his summers doing light work in a garden. He had marked difficulty in tying up flowers about one year ago. He passed, however, an insurance examination at this time, increasing his policy. His weakness slowly increased. In February, 1923, he became dizzy and fell. There was no fracture and he left the hospital in two days. He has fallen twice since then. Shortly after this, he noticed that he had difficulty in controlling his emotions: he would rather "overdo the part" and laugh or cry longer and louder than was consistent with the occasion. There were occasional choking spells and swallowing was slightly affected. Except for slight discomfort in the right shoulder, there was no pain. The voice gradually became deeper and of nasal quality, growing weak during the day and giving out during the evening. He found difficulty in feeding himself, and his gait became stiff and awkward.

Examination showed some moderate general weakness and slight bowing of the legs. His back was straight and there was no enlargement of the head. The pupils and cranial nerves were normal. There was slight if any atrophy of the tongue, but a rather coarse tremor was present. All the intrinsic muscles of the hands were atrophic with corresponding loss of strength. These muscles showed reaction of degeneration. The arm reflexes were pathologically increased and about equal. Numbness of the finger tips was complained of but no objective signs to prick, touch, hot or cold were found. The blood pressure was 140 systolic, 70 diastolic without evidence of peripheral sclerosis. The sphincters were not involved. The legs were mildly spastic with an equal increase in the reflexes, including bilateral clonus and Babinski sign.

Lumbar puncture yielded 10 c.c. of clear, colorless fluid; pressure 160 mm., pulsations and jugular compression within normal limits; cells, 1 per cubic millimeter; protein, 31 mg. per 100 c.c. Wassermann reaction negative. Blood examination revealed Wassermann reaction negative; white cells, 6,800; hemoglobin, 65 per cent.; red cells, 4,040,000; smear: polymorphonuclears 62 per cent., lymphocytes 30 per cent., large mononuclears 4 per cent., eosinophils 1 per cent.,

basophils 1 per cent.; the red cells showed moderate variation in size but none in shape, no achromia, basophilia, or stippling.

The diagnosis first made was amyotrophic lateral sclerosis. Because of mild pain in the shoulders, bursitis was suspected and roentgenograms were made of this region. The appearance of the head of the humerus suggested Paget's disease and the pictures of the other bones confirmed the diagnosis as shown in the following report.

Roentgen-Ray Examination.—The plates show a distinct variation from normal in the upper end of the humerus, the scapula, skull, pelvis, spine, tibiae, and femora. The bones are enlarged and somewhat irregular in outline with coarse irregular trabeculations and narrowing of the medullary canal in the long bones. The appearance is typical of Paget's disease.

Comment.—Amyotrophic lateral sclerosis was first described by Charcot and Joffroy (*Archives de physiologie normale et pathologique*, **2**:354, 629 and 744, 1869). Gordon Holmes, in 1909, (*Review of Neurology and Psychiatry* **7**:693, 1909) published some careful work on ten postmortem cases and emphasized that the lesion, from the pathologic point of view, was diffuse and not confined to the lateral columns and the anterior horns. Paget's original description and pictures of osteitis deformans (*Medico-Chirurgical Transactions, London* **60**:37, 1877) are classical. Morton Prince (*Transactions of the Association of American Physicians* **17**:382, 1902) was not able to demonstrate definite lesions in the nervous system, and very few changes have been found since that time. One or two cases of Paget's disease, however, have been described with posterior column sclerosis, and one with chronic myelitis. Marie and Léri (*Bulletin et memoires Société médicale des hopitaux de Paris* **43**:904, 1919) have published a case of Paget's disease, which at necropsy showed unsuspected syringomyelia from the first lumbar to the second dorsal sugment. In Charcot's second case there seems to have been a definite cavity of syringomyelia which shows in one of his drawings.

I was not able clinically to demonstrate Paget's disease in my patient, although when studied carefully after the roentgen-ray examination, there was noted slight bowing of the legs and arms, but no definite deformity of the skull. The roentgenograms of the long bones were remarkable, and showed the changes associated with Paget's disease.

DISCUSSION

DR. E. W. TAYLOR: I entirely agree with Dr. Viets in his diagnosis. The patient presented a perfectly typical picture of amyotrophic lateral sclerosis. It is hard to see how changes in the bones could produce this condition except perhaps by pressure causing changes in the cord. Of course there are sometimes changes in the vertebrae as well as in the long bones, and exostoses might occur and lead to pressure in the cervical region. The changes about the cranium and skull in this case are noteworthy, and it is possible they help to account for the conditions in the tongue and in the spinal cord which proclaimed themselves as typical amyotrophic lateral sclerosis.

DR. VIETS: Typical Paget's disease will show absorption of bone and laying down of new bone of irregular character. With regard to Dr. Taylor's point that the vertebral column might have affected the spinal segments, it is true that the vertebrae showed changes typical of Paget's disease, but there appeared to be no more changes in the seventh cervical and first dorsal vertebrae than in the other parts of the spinal column. Pressure was ruled out by the procedures

carried out at the time of the lumbar puncture. There was no evidence of subarachnoid block. There appeared to be some intrinsic disease of the cord. That the changes may be neurogenic has been the theory advanced by Dr. Prince and many others, and is based somewhat on the analogy of changes found in syringomyelia and tabes dorsalis; but many cases of Paget's disease have been analyzed since Dr. Prince's work, and very careful work done in the last decade on the pathology of the nervous system, without confirmation of the neurogenic theory. The case reported by Marie and the one described here might offer some evidence substantiating a theory of neurogenic origin.

OBSERVATIONS IN VENTRICLE AND CISTERN PUNCTURES. Dr. A. H. Ruggles.

For the past two and one-half years, we have been interested in cistern puncture as described by Ayer as an avenue of approach in the treatment of general paralysis. We have been impressed by the simplicity of the technic, by the lack of discomfort to the patient, and by the theoretical advantages of the more direct approach to the seat of the disorder. In applying intracisternal treatment in general paralysis, we have directed attention, as have a number of other workers to the question of the passage of the cerebrospinal fluid from above downward and the possibility of passing fluids from the cistern into the ventricles. At the time we did this work we were not aware of Solomon's work but we wish to offer certain observations, in most part confirming results of other workers.

REPORT OF CASES

Case 1.—F. H., aged 40, married, was admitted May 1, 1922, with general paralysis of a duration of two years.

April 14, 1923, under local anesthesia (procain from ¼ to 1 per cent.) an opening was made in the right parietal region by means of Hudson burrs; after this a needle was inserted into the ventricle and a cistern puncture done, without draining the cistern, and 20 c.c. of a weak phenolsulphonephthalein solution injected to see if it could be made to flow upward into the ventricle. The ventricular fluid was allowed to drain off, but after fifteen minutes none of the solution was recovered; then 20 c.c. of saline was allowed to run into the ventricle by gravity and this seemed slightly to increase the flow from the cistern needle. Nearly all of the phenolsulphonephthalein was recovered from the cistern. The wound was closed in the usual manner and the patient returned to the ward in fairly good condition.

April 20, 1923.—In the first twenty-four hours after operation, the patient's temperature went up to 104 F., but with no corresponding increase in the pulse rate. The pulse was weak, however, and the night of the operation he was given 400 c.c. of saline solution intravenously and an ampule of digifolin. The quality of the pulse improved and during the next seventy-two hours his temperature fell to normal, and his pulse rate became normal and of good quality. He is now in approximately the same condition as before the operation.

April 23, 1923.—Cistern puncture was done and about 20 c.c. of fluid removed. It was examined for phenolsulphonephthalein and none was found.

April 30, 1923.—Ventricular puncture was performed, about 5 c.c. of fluid removed and the needle left in place. A cistern puncture was then performed. A gravity cylinder, containing 20 c.c. of saline solution to which had been added 1 c.c. of a neutral phenolsulphonephthalein solution (prepared after Dr. Dandy's formula), was connected with the ventricular needle and 10 c.c. allowed to run

in. The stylet was removed from the cistern needle and two minutes later the dye was recovered in the cistern fluid in very noticeable concentration; about 20 c.c. was removed by the cistern needle and then the cistern needle was withdrawn. A lumbar puncture was then performed and 10 c.c. more of the original solution was allowed to run into the ventricle. In twelve minutes it appeared in the lumbar fluid in very dilute quantities. About 15 c.c. of spinal fluid was recovered by the lumbar needle. It is possible that the dye would have been recovered earlier and in greater concentration had not the cistern been so completely drained. The patient was in good condition and complained of no discomfort after this procedure.

May 2, 1923.—Ventricular puncture was performed and slightly blood tinged fluid was obtained. Cistern puncture was then done and slightly blood tinged fluid was obtained here also. Twenty cubic centimeters of a solution of phenolsulphonephthalein was allowed to run into the cistern by gravity (1 c.c. to 20 c.c. saline solution). The head of the table was lowered, the stylet was removed from the ventricular needle and in fifty seconds the dye was obtained in such concentration that it was very noticeable, even with the blood tinged fluid. The cistern needle was removed. About 25 c.c. of fluid was taken from the ventricle, all of which was strongly colored with the dye. The needle was then removed from the ventricle. Lumbar puncture was done and bloody fluid was obtained under very slight pressure. This pressure was increased when the foot of the table was lowered. Almost immediately the fluid became dye stained.

May 5, 1923.—Lumbar puncture was done and a straw colored fluid was obtained.

May 7, 1923.—Lumbar puncture was performed and about 60 c.c. of straw colored fluid was removed, which, however, was not so deeply colored as that obtained at the last puncture; the addition of sodium hydroxid showed no color which would suggest that any of the dye-stuff still remained in the subarachnoid space.

May 9, 1923.—Cistern puncture was performed and 5 c.c. of dye-stuff was allowed to run into the cistern by gravity, but as no more would run in by gravity, 15 c.c. more was forced in by syringe. There was no change of pulse or respiration during the procedure. The head of the table was lowered. Twenty-five minutes afterward the ventricle was punctured and about 4 c.c. of clear fluid was obtained. On draining the ventricle, dye-stuff was recovered thirty-four minutes after its injection and was obtained in considerable quantity. Lumbar puncture was performed and dye stuff was obtained immediately in the fluid there but the pressure was very low—probably on account of the removal of ventricular fluid. It is our opinion that while dye-stuff will flow from the cistern to the ventricle when the ventricle is drained, no substance can be passed into the ventricles of the brain without drainage of the lateral ventricle.

Case 2.—E. A. K., aged 45, single, was admitted, June 15, 1923, the diagnosis being general paralysis with a duration of eight months.

Sept. 12, 1923.—Yesterday, the patient was operated on under ether anesthesia and an opening made in the occipital region of the skull according to the route suggested by Dandy. It was found that to enter the ventricle, the needle needed to be directed downward almost toward the point of the ear. In this direction the ventricle was entered without particular difficulty. Seventeen cubic centimeters of serum, prepared according to the Swift-Ellis method, to which had been added 1 c.c. of neutral phenolsulphonephthalein, was injected into the ventricle. The opening was closed. Cistern puncture was then per-

formed and a few drops of colored fluid obtained and the needle immediately removed. This shows fairly definitely that fluid remedies injected into the ventricle will immediately pass to all parts of the ventricular system. The patient this morning shows no untoward or alarming symptoms; temperature, pulse and respiration are normal.

Oct. 16, 1923.—Since the last note, the patient has had nine ventricular punctures. Practically no difficulty has been experienced in entering the ventricle and the patient has suffered from no untoward symptoms following treatment. He has been a great deal quieter, showing a gradual lessening of activity since the time of operation. He sleeps fairly well at night; his appetite is good and he has had a gradual return of strength since the operation. His memory is better. He shows some flight of ideas, but this is not nearly so marked as previously.

Comment.—In the first case reported, we were much impressed with the difficulty of passing fluid from the cistern into the ventricle, unless the ventricle puncture was made and the pressure in the ventricle first lowered; then it was possible to obtain the dye stuff put into the cistern from the ventricle in a comparatively short time; but without first lowering the pressure in the ventricle, this flow was very slow and very limited. It is our belief, therefore, that intracisternal remedies will not be conveyed directly to the ventricle except in limited amount, and that treatment given into the ventricle quickly circulates to the cistern below. Another point that we have determined lately is the ease of approach to the lateral ventricle by the method of Dandy as described in *Surgery, Gynecology and Obstetrics,* May 1923.

In the second case reported we have already given nine ventricular treatments through the occipital opening and have had, much to our surprise, improvement in the case in which this treatment was employed, although such improvement was hardly expected as he had previously had prolonged intracisternal treatment without noticeable change. In approximately two hundred cistern punctures done since those reported by McCusker at Butler Hospital, we have had no untoward results; there has been less discomfort to the patients than in a like number of lumbar punctures, and we have an avenue of approach more closely associated with the seat of the disorder than is the lumbar region.

In those cases in which it is deemed advisable to give ventricular treatment we would suggest, as the result of our limited experience, the occipital route of Dandy as offering no greater difficulty of technic and possibly greater ease in entering the ventricles. Our whole effort in the treatment of general paralysis has been, as far as possible, to study all the methods rather intensively, perfecting our technic so that in patients resistant to one type of treatment we might have others to employ and continue treatment, in most of our cases, over a long period by the various methods as indicated. We hope to pursue our investigation. At the present time we are encouraged with the results in our cases rather than the contrary.

DISCUSSION

Dr. A. T. Wyatt: From studies I made, I found the anterior horn of the ventricle was very small from above downward, and immediately underneath the surface are the basal ganglions, which are extremely likely to be punctured. The posterior horn is not always present; in some cases it is absent entirely. It would seem from the sections studied that the best way of getting to the ventricle would be from a lateral position one inch above the orbital level and two-thirds of the distance from a line drawn through the midline posteriorly,

and one through the external auditory meatus. The cistern is easier of access than the ventricle. The patients suffer less with headache from cisternal puncture than from lumbar puncture, and do not complain of as much pain at the time of puncture. This method is not new; it has been done by Dr. Cushing. I merely emphasize the advisability of going in from that direction.

Dr. J. B. Ayer: I have seen this method of ventricle puncture used both by Dr. Cushing and Dr. Mixter, and I think by Dr. Frazier. The results of Dr. Ruggles are in line with those of Solomon who finds a less concentrated fluid in the ventricles as compared with that in the subarachnoid spaces, and with those of Dandy who shows experimentally that most of the fluid is produced in the ventricles, and with recent studies of Weigeldt who finds the pressure in the ventricles a little higher than in the surrounding subarachnoid space. We have then considerable evidence that serum does not easily enter the ventricles from subarachnoid injections, and on the other hand that serum administered directly into the ventricles may be promptly beneficial. The conclusions appear obvious.

Dr. H. C. Solomon: We found, a little differently from Dr. Ruggles, that there was a little upward movement of the dye. The downward movement was more marked, but there was some upward current. I am interested in Dr. Ayer's difference between the ventricle and cistern pressures. We have made a number of experiments of similar type, taking the lumbar and ventricular pressures simultaneously, and found they were identical in many instances as nearly as we could tell. If we moved the patient so that his head was lower, the ventricular pressure would rise and the lumbar fall, nearly simultaneously. With the withdrawal of fluid from one place or the other, the difference in pressure is simultaneous as nearly as we could determine.

As to where to puncture, it is a very simple procedure wherever you go in. We have used the frontal, going into the anterior horn, where the ventricles are dilated. It is necessary to use a blunt needle. Cistern punctures are rather easy to do, and the patients rarely complain of headache; much less than in lumbar punctures. Notwithstanding that many thousands have been done without difficulty, I still feel some trepidation and anxiety when doing that puncture. With regard to serum, I should say that the patients do not like it. Our patients object to it a great deal more than they do to ventricular or lumbar injections.

Dr. Percival Bailey: I think Dandy simply does what we have seen Dr. Cushing do, for many years, during a cerebellar operation. As a matter of fact, the posterior route is a very bad way to reach the ventricle because the ventricle is far away from that point, and one is aiming at a very small part of the ventricle. I think it makes little difference where one punctures the ventricle. We never take measurements because if one puts a needle almost anywhere on the upper surface of the head, one will hit the ventricle provided the needle is introduced perpendicular to the surface. If the ventricle is dilated, one cannot miss it. I have never seen trouble from puncturing the choroid plexus. Dr. Davis of Chicago, who is present this evening, can doubtless tell us about the posterior horn.

Dr. Loyal E. Davis: Retzius, many years ago, called attention to the fact that in about 33 per cent. of all human brains the posterior horn of the lateral ventricle is rudimentary and resembles somewhat that of the dog. I have recently confirmed this observation by filling the ventricles of properly hardened brains with mercury and then taking roentgenograms of the specimens. This will explain the difficulty experienced at times in performing a ventricular punc-

ture through the occipital horn, particularly by those not well acquainted with the normal anatomy of the ventricles. I quite agree that ventricular puncture at almost any point in the cerebral cortex overlying the ventricles should prove quite simple at all times and it makes little difference as to the site of puncture.

Dr. F. J. Farnell: Merely as a matter of record relative to this ventricular procedure and the results derived therefrom; four or five years ago I treated six cases of general paralysis by the ventricular route. All were treated over a period of several months. I injected the serum into the anterior horn in all cases. Two of these cases have since died, one is now in the state hospital for the insane, and three are attending to their duties at home. I had the pleasure of seeing two of the patients a few months ago, and both are in fairly good mental and physical condition. Those two patients have not received any form of antisyphilitic treatment during the past two years.

Dr. Ruggles: The anatomic discussion I do not feel qualified to enter into. If we were to take the textbook plates and some work Dr. Wyatt has done on frozen sections, it would seem that the posterior horn was easier to enter than the anterior horn, and the distance is somewhat less; we have felt, therefore, that the posterior route offered fully as simple and certainly no more dangerous a procedure than the anterior route. I agree with Dr. Bailey that it is a simple procedure no matter which way one may enter.

Regarding Dr. Farnell's report as to the treatment: We have been following this a good while, and have spent much time and medicine on treatment, and we feel inclined to go on with it. I cannot say we have cured any patient. Some remarkably improved patients went out to work two or three years ago; two are now dead; but every year it seems to me we send more patients back to their jobs, and if we succeed only in keeping more of those to whom we give intensive treatment somewhat longer at work, it is worth while. To illustrate: a patient with an active period of general paralysis, was able following treatment, to settle up his business, which amounted to three hundred thousand dollars. He sold out, invested his money himself, and though now ill again he was able to protect himself and his family.

It has been said that the good results of the treatment of general paralysis now being reported are due simply to the fact that physicians and nurses take more interest in them, see them and examine them more often. If that is the result, we had better keep on treating them. I believe with Dr. Farnell that some of the cases we have treated have done better than any we saw before treatment. One man at the present time has been employed since early last spring on very difficult work as a machinist. When we saw him two months ago he was doing good work and getting on very well. Another man had his last treatment two years ago, and is still earning his living as a stone setter.

SCHWEIZER KÄSE GEHIRN (SWISS CHEESE BRAIN). Dr. Hugo Mella.

This brain may recall perhaps the war experiences of some of the members. It is from a man, aged 49, who was first seen in March, 1922. A diagnosis of cord tumor was made. Operation was performed by Dr. W. J. Mixter, and a tumor was found in the center of the cauda equina. It was removed without any apparent destruction of the nerve roots. Recovery was excellent except for slight motor disturbance in one leg. The patient got on well until Aug. 10, 1923, when he quite suddenly became unconscious and was taken to the Newburyport hospital. At that time he showed indefinite paresis of the extremities

with rigidity of the neck. Two days before death he developed a severe phlegmon of the face extending from the hair line down over the forehead to the upper lip. Dr. Ayer punctured his cisterna. He died August 17.

A necropsy limited to the head and cord was performed seven hours post mortem. The upper half of the face was extremely edematous, of such degree that the eyes could not be opened. There was no crepitation in this area. The scalp and dura were not adherent to the calvarium. On opening the cranium the dura over the left hemisphere was found very tense, whereas that over the right hemisphere appeared to be under normal pressure. On reflecting the dura over the right hemisphere the gyri appeared normal, whereas on the left, the gyri were flattened to such an extent that the sulci appeared as mere lines. The pia was hyperemic over both hemispheres.

On tipping back the brain to sever the optic nerves, the left occipital lobe ruptured and a clot of dark blood about 3 inches in diameter was extruded; accompanying it were about 2 ounces of thick, greenish, purulent substance. The brain was then removed and placed in a solution of formaldehyd. The cord was removed with difficulty owing to the scar of the operation, but was found intact.

After fixing the brain for six weeks, transverse sections were made, when this striking condition was found. The brain has the appearance of swiss cheese, being "full of holes." Similar holes were also observed in the cerebellum and pons but not in the cord. Sections of the brain tissue show clumps of what are evidently gas forming bacilli. In the cortex were found: ameboid glia cells, marked proliferation of glia nuclei, neuronophagia, and clumps of fat in the neurons. No perivascular exudate was found in the sections studied. In the cord the only changes observed were occasional clumps of fat in the anterior horn cells.

I have here also several photographs of a brain similarly invaded with gas forming bacilli, which Dr. E. W. Taylor had in his collection.

DISCUSSION

Dr. Percival Bailey: When I was an intern there came into the Cook County hospital a house servant who had had an abortion performed a few days before. Her employer took her to a physician who found a violent uterine infection. She was semicomatose on admission. She developed very definite crepitation in the subcutaneous tissue practically all over the body. She died and the necropsy was reported by Dr. Hassin in the *Archives of Neurology and Psychiatry* with an extensive discussion of the condition. At necropsy the brain was definitely crepitant. I do not remember how long postmortem the necropsy was performed. There was much discussion as to whether the change was antemortem or postmortem. Dr. Hassin believed the former and so stated. I agree with this conclusion, though a considerable time elapsed before the brain was taken out; I am satisfied also that the presence of these lesions in the nervous system was not due to fixation in formaldehyd. In this case the same organisms that Dr. Mella found in his case were present.

Dr. Raeder: In the Waverley series we had a case which we called the cheese brain, but it was apparently due to a different cause. The patient, about 9 years of age, was studied by Dr. W. T. Councilman and is reported in the second volume of the Waverley Research Series. There was a perivascular growth of a loose cellular tissue with perivascular edema and some mononuclear infiltration, and it was connected with considerable hydrocephalus. The Wasser-

mann test was not made in that case, but most of the histologic evidence pointed to syphilis as the cause. While this case gave the same picture, I noted that in Dr. Mella's specimen the holes are fairly general in the white matter and spare the cortex; that is the same picture that we had in our case; but while the condition in our patient was chronic, in this case, I take it, it was acute, although the gross picture is very similar.

Dr. F. H. Packard: I have seen a number of such brains and I think that in the large state hospitals they are not infrequent. Some years ago we had such a case at McLean Hospital which was reported by Dr. Emma Mooers. The patient was a well advanced general paralytic. He rather suddenly became seriously ill; there was great distention of the abdomen; he became stupid and died. At necropsy, within twenty-four hours, the chest and abdomen were crepitant; in fact, the body was more or less so everywhere except on the scalp. Holes were seen throughout the brain on section. There were similar holes in the liver and spleen and microscopically they could be seen in the kidneys and heart. I think that these changes are generally regarded as postmortem; one reason for this being that the cavities have no membranous lining. Such cases were first described in 1870, and there was for some time considerable controversy as to whether or not the changes were antemortem or postmortem.

Dr. Percival Bailey: In the case of bacillus infection that I saw, there was a definite pathologic membrane surrounding some of these areas, and the areas were full of gas bacilli.

Dr. F. J. Farnell: I would like to ask Dr. Mella if there was any pathology in the brain aside from the abscess; and also whether the fat that was seen about the area of necrosis might not be the remains of a large group or area of fat cells that had been destroyed. A recent report from England in relation to fat definitely states that formaldehyd acts on some tissues and with some organisms by removing the fat and leaving a definite loss or changed area such as is seen in these pictures.

Dr. D. J. MacPherson: May I ask whether in the investigation of the first brain it was noticed if these holes were around the vessels?

Dr. J. B. Ayer: This patient presented a clinical picture of meningitis. I was asked to see him with a view to treatment via the cisternal route because lumbar puncture had failed to yield fluid. A blood-tinged fluid was obtained from the cisterna magna, which showed an increased number of cells, though not an excessive number, but no organisms either on direct film examination or on culture. Antimeningococcic serum was given by this route, and repeated the next day, so strongly did we feel that a diagnosis of meningitis was correct. I observed no crepitation of the tissues on either day. In view of the possible infection with gas bacillus by the two cisternal injections it should be stated that all of the instruments used were boiled immediately previous to puncture. The serum administered on the first occasion was from the Mulford laboratories, on the second from the Massachusetts State Board.

Dr. Mella: The fat I spoke of was in the neurons of the anterior horns of the cord. As to the brain Dr. Raeder spoke of, I may be mistaken but I thought that was grouped under the degeneration we see in the idiot now and then. It is probably due to a vascular lesion. I cannot find that these cavities are related to blood vessels; it is apparently nearly a diffuse involvement of the brain by this organism. It did not involve the cortex to any great extent but was not confined entirely to the white matter.

CHICAGO NEUROLOGICAL SOCIETY

Regular Meeting, November 15, 1923

JULIUS GRINKER, M.D., *President, in the Chair*

AN ADJUSTMENT OF ADOLESCENCE. DR. RALPH C. HAMILL.

The evolution of the ideas of childhood to those of the second half of the second decade is beset with many difficulties. One of these is the difficulty of adjusting the infantile and childish sexual conceptions to those of the young adult. The child's ideas are purely physical and sensual. Those of the adult are dominated by the element of reproduction; the child's are lewd, the adult's mixed with respect. The process of reconciliation of lewdness with respect, of the sensuous with the reverential, is for many minds difficult. Most men feel that they must assume familiarity with sexual experience if such experience is not actual. Hence, there is considerable difficulty in eliciting an expression of fear concerning sexual temptations or impulses. The usual attitude is that they "know all about that stuff and there is no use talking about it." However, there is something to the idea that, with many men, intercourse has been sought as a cure for masturbation, in which case the unpleasant mental attitude concerning masturbation is carried over into intercourse. This does not represent the kind of progress desired.

The dreams of four patients were cited to show that in spite of the avowed claim that the patient's attitude toward sexual experience was all that it should be, there was in the background the childish fear of sexual temptation.

The first patient had dreamed that he was in a hotel over the entrance to which was the date 1860, the date of his dead mother's birth. In front of the hotel were two cowpens, in one of which were some Brahma cows and in the other two Brahma bulls. The hump on the Brahma cattle suggested the papoose borne on its Indian mother's back; suggested the idea he had had while riding the cattle range of marrying an Indian because she had no foolish ideas about sexual refreshments. He is engaged to a girl on the Atlantic coast, an expression of his effort to get as far as possible from the Indian woman. The two bulls suggested his father and himself and he then severely criticized his father's conduct in keeping a woman to whom the widower was not married. In connection with this dream he spoke of the perfect naturalness of his own attitude toward fornication; he had been to a prostitute a few days before. However, he also said in connection with the idea of marrying a full-blooded Indian woman that he had come to consider such a step too radical; had compromised on a half-breed, then on an octaroon, and was now engaged to a girl on the Atlantic coast. He expressed much apprehension of his ability to measure up to eastern standards of conduct.

The other cases showed similar mechanisms in their dreams: The attraction of the physical with a tendency to emphasize the bestial set over against expressions of self punishment.

HEADACHE AND VERTIGO IN URICACIDEMIA. DR. WILLIAM H. HOLMES.

This article is printed in full in this issue of the ARCHIVES.

SOME SURGICAL COMPLICATIONS OF VON RECKLINGHAUSEN'S NEUROFIBROMATOSIS.

Dr. Dallas B. Phemister.

Surgical complications in von Recklinghausen's neurofibromatosis result mainly from three things: (1) malignant degeneration in the neurofibromas; (2) pressure of tumors on brain or cord, and (3) marked overgrowth of involved part producing either mechanical or cosmetic disturbance. Malignant degeneration of a neurofibroma is fairly common. It is most frequent in tumors situated on the nerve trunks of the central nervous system, but is seen occasionally in those of the sympathetic system. Adrian estimated that one case in twelve died of sarcoma arising in a neurofibroma. Although the skin is practically always involved with fibromas or pigmented spots or both, it has not been reported as the seat of a sarcoma. I shall report three cases of sarcoma arising in the nerve in patients with neurofibromatosis.

Case 1.—R. F., a woman, aged 35, had had pigmented spots and soft tumors in the skin and lumps in the subcutaneous tissues since childhood. The mother, one brother, one sister and her only son had von Recklinghausen's neurofibromatosis. For nine months she had had a gradually enlarging swelling on the back of the left thigh, which had become very painful. Examination revealed a small woman with intelligence considerably below the average. There was left internal strabismus. The skin was the seat of pigmented spots and soft sessile tumors, which were irregularly distributed and most extensive on the back of the trunk. There were hard nodules, mostly of small size, to be found along the vagus trunk in the neck and the brachial plexuses in the arms. There was a similar egg-sized tumor just below the head of the left fibula. There was a large, firm swelling occupying the back of the left thigh, extending from gluteal fold to popliteal space. Left hip joint amputation was performed. Dissection of the limb revealed numerous small and large neurofibromas on the branches of the sciatic nerve and a large oval swelling 9 inches (23 cm.) in length on the posterior tibial division of the nerve. The posterior surface of the lower part of the shaft of the femur had been eroded and directly invaded by tumor. Microscopic sections taken from the periphery of the tumor revealed a round and spindle cell sarcoma without the presence of nerve elements. The patient died nine months later from pulmonary metastases.

Case 2.—J. W., a man, aged 31, had had pigmented spots and soft tumors in the skin since childhood. A tumor on the anterior surface of the right arm had been growing gradually for two years. There was no family history of neurofibromatosis and the patient was of average intelligence. On examination, he had a right internal strabismus. There were numerous soft neurofibromas and pigmented spots in the skin, particularly of the trunk. No neurofibromas could be found along the course of the main nerve trunks. There was a large spherical swelling on the anterior surface of the right arm, which was tense and movable on the bone. Intrathoracoscapular amputation was performed by Dr. C. B. Davis. The tumor proved to be a sarcoma of the right internal cutaneous nerve. Death occurred three years later from metastases in the chest.

Case 3.—E. T., a woman, aged 44, had had very extensive pigmented areas and a few small tumors of the skin of the abdomen since childhood. Her intelligence was of high grade and there was no family history of neurofibromatosis. A gradually enlarging tumor had been present on the anterolateral aspect of and above the right elbow for two years. Examination was negative aside from the extensive pigmentation and small neurofibromas in the skin of the abdomen, and a large, firm tumor of the soft parts along the

course of the right musculospiral nerve at the elbow. After a massive roentgen-ray treatment the tumor was excised locally. It was found to spring from the musculospiral nerve. Microscopically it was a round cell sarcoma.

Verocay claims that these tumors are not true neurofibromas, but that they arise from the sheath of Schwann, and he terms them neurinomas. That some of the sarcomas come from the cells of the sheath of Schwann is undoubtedly true, but others are derived from the connective tissue element of the nerve. These three tumors seem to be of the primary connective tissue type.

Pressure on the brain or spinal cord may be the result of endothelioma of the meninges, glioma or neurofibroma. Meningeal endothelioma in von Recklinghausen's disease may be single or multiple. When single, the tumor may be large and the overlying bone may be invaded with the production of hyperostosis, as sometimes occurs in endothelioma alone. Glioma of either brain or cord may be a part of the picture, but the tumors are rarely of such size as to cause pressure symptoms. Tumors of the nerves within the bony case of the central nervous system are the commonest cause of pressure symptoms. Within the skull the eighth nerve is most frequently involved, and a considerable percentage of cerebellopontile angle tumors belong to the class of neurinomas.

Tumors of the nerves within the spinal canal are less common. They may be situated intradurally, but may be located outside the dura. The following is a case of this type:

Case 4.—The patient, a man, aged 32, had had pigmented spots and soft tumors of the skin since childhood. Two brothers had von Recklinghausen's disease. The patient had had gradually increasing motor paralysis of the body and limbs, most marked on the left side, for four years. Examination revealed a man of small stature and of low grade intelligence. The skin of the trunk and to a less extent of the extremities contained numerous pea to dollar sized brownish pigmented spots and a few soft neurofibromas. He was paretic from the head downward, the strength of the left extremities being about four-fifths normal, while that of the right was about one-half normal. The reflexes of the extremities were increased and a bilateral Babinski sign was present. The abdominal muscles were greatly weakened. The diaphragm and the muscles of the abdominal wall were weak, as were also the neck muscles, except the sternocleidomastoids. These were considerably hypertrophied and stood out markedly in the neck during inspiration, and it was evident that breathing was carried on mainly by them. There was slightly diminished sensation in the left side of the body, but on the whole it was everywhere remarkably well preserved. The diagnosis made was "Neurofibroma compressing the upper cervical cord above the level of the third cervical segment." Under local anesthesia the upper cervical spine was exposed and a dumb-bell shaped tumor was found, one portion of which projected from the right second intervertebral foramen. After removal of the arches of the first and second vertebrae, the portion of the tumor within the canal was found to lie anterior to the meninges and cord. After cutting the proximal and distal ends of the right second cervical root, the tumor was removed. It measured 6 cm. in length. The two portions of the dumb-bell shaped tumor were of equal size and averaged 2.5 cm. in diameter. Microscopically the tumor was a neurofibroma and appeared to be entirely of connective tissue origin. Following the operation, the patient's paralysis gradually improved and now at the end of six months he is able to walk, although some spasticity is present.

Growth anomalies resulting in mechanical or cosmetic disturbances are extremely variable in type. Facial hemihypertrophy is a fairly common form, and in it the other manifestations of von Recklinghausen's disease are usually slight. Plastic operations may be indicated for reduction in size of the affected portions of the face and restoration of facial symmetry.

CASE 5.—This patient, a boy, aged 6, had left sided facial hemihypertrophy, affecting especially the left upper eyelid, cheek and temporal regions, since birth. There were bony bulging of the temporal region and elephantiasis-like enlargement of the eyelids, particularly of the upper lid. There were several large and small pigmented spots scattered over the skin of the trunk, but no subcutaneous neurofibromas. The redundant portion of the upper lid was excised and the bone of the left temporal region was removed, producing marked improvement in appearance. Microscopic examination of tissues from the lid revealed a loose connective tissue, containing a few irregularly coursing nerve fibers.

Localized giant growth affecting the extremities in abortive cases of von Recklinghausen's disease is fairly common. The picture may simulate elephantiasis, in which the soft parts are markedly enlarged but the skeleton remains unchanged, or there may be increase in length of the bones of the extremity, as in the following:

CASE 6.—The patient was a girl, aged 10, whose left lower extremity had been enlarged and longer than the right since birth. At the time of examination it measured 1½ inches (3.8 cm.) longer than, and the average circumference was one and one-quarter times that of the unaffected side. There was extensive pigmentation of the left thigh, with soft neurofibromas in the subcutaneous tissues above the left knee. There were a few pigmented spots on the skin of the body, but no neurofibromas. The deformity produced a marked limp and curvature of the spine. Such a localized hypertrophy should be treated by obliteration of the lower epiphyseal line of the femur, performed at the proper age to make the two extremities of equal length at the time of cessation of bone growth. In this case the operation was refused.

DISCUSSION

DR. PETER BASSOE: I have been much interested in von Recklinghausen's disease since I encountered a case in a child about nine years ago. There were symptoms both of brain tumor and spinal cord tumor, with numerous cranial nerve palsies and headaches as well as paralyses and sensory disturbances in the legs that could only be explained by separate brain and cord lesions. There were only two nodules that could be felt externally. There was one in the neck that had been interpreted as a tuberculous gland and one or two on the chest. The internal involvement was very extensive. There were neurofibromas on practically all the cranial nerves, including both auditory nerves, and yet the hearing had not been abolished. There were at least 100 tumors in the spinal canal, and apparently tumors inside of the spinal cord, but on dissecting them we found they were tumors of the posterior roots that had grown into the cord. In the interior of the brain there were small foci with peculiar cells, most of them neuroglia cells, and these little lesions resembled those that are found in so-called tuberous sclerosis, a rare disease.

There have been combinations, as Dr. Phemister said, of so-called endothelioma of the meninges with von Recklinghausen's disease and of glioma of the retina and von Recklinghausen's disease. I believe there have been cases

even with all these tumors together, which is a strong argument in favor of the view that all of these tumors are due to some early embryonal disorder.

In cases of tuberous sclerosis we often have a great many other malformations and rare tumors of the skin, retina, heart muscle, kidneys, etc. For that reason and on account of the histologic structure of a great many of these neurofibromas it is probably reasonable to say that they are due to some disorder starting in fetal life before the nerve tissue has been fully differentiated.

NEW YORK NEUROLOGICAL SOCIETY

A Joint Meeting with the Neurological Section of the New York Academy of Medicine, Nov. 13, 1923

E. G. Zabriskie, M.D., and Henry A. Riley, M.D., *Presiding*

SYMPOSIUM ON EPIDEMIC ENCEPHALITIS

I. CASES FROM THE NEW YORK NEUROLOGICAL INSTITUTE

Dr. E. G. Zabriskie: Case 1.—The patient, a middle aged woman, had a typical onset with high temperature and delirium; she then went into a phase with an acute bulbar syndrome and was unconscious for six weeks. The temperature was 102.4. There was difficulty in swallowing with complete bilateral facial paralysis and respiratory disturbance; she suffered very little pain, but was left with considerable deltoid paralysis of both arms. The disease has picked out different groups of muscles; on the right is seen better extension of the forearm than of the fingers; on the left there is lack of extension of the forearm and good extension of the fingers. The cranial nerves have completely recovered, and she is making fairly regular progress between the upper dorsal levels.

Case 2.—This patient presents several unusual features. The young woman was taken ill four years ago and there was a typical course. She was ill for six or eight months with lethargy, diplopia and fever. She had an inconstant fine tremor from which she apparently recovered so completely that she married. Shortly after marriage she became pregnant. Six months after the birth of the child she began to show the condition from which she is now suffering: tremor of the left arm and a peculiar facial expression, marked by constant depression of the lower jaw which gives an appearance like a yawning reflex. She also has gained about 60 pounds (27 kg.) in weight, which is still increasing.

DISCUSSION

Major Jarvis (by invitation): How frequent are the yawning movements? Does she sleep profoundly, or does this motion keep up at night?

Dr. Mailhouse: Has the patient been influenced by any form of treatment?

Dr. E. G. Zabriskie (closing): She sleeps fairly well. I have rarely seen the full yawning reflex. I have seen involvement of the platysma, of the sternomastoids, and of the diaphragm, but most frequently there is simple dropping of the jaw with partial involvement of the sternomastoids. In this case there is partial closure of the right eye. It is difficult for me to determine how much

is voluntary movement to overcome the disability. She apparently made a complete recovery originally. No form of treatment has been of use.

DR. J. W. STEPHENSON: CASE 3.—This man, aged 35 years, watchmaker by occupation, whose remarkable improvement was considered to be the result of a definite line of therapy, entered the hospital March 18, 1922, with violent myoclonus of the right upper extremity, the right abdominal muscles and the left lower extremity. So severe was the myoclonus that it was necessary to place boards on the side of the bed to prevent him from throwing himself out of bed. He was seen independently by several observers all of whom agreed on the diagnosis; namely, epidemic encephalitis.

On entering the hospital the patient's temperature varied from 100 to 102. March 23, administration of strychnin nitrate, 1/30 grain (0.002 gm.), with pituitary extract (pituitary liquid [Armour & Co.]) 7½ minims (0.5 c.c.) was begun. His temperature at once began to drop and in five days was normal. Within forty-eight hours after beginning this therapy there was marked subsidence of the myoclonus which completely disappeared in four days. It was then observed that the patient was developing a parkinsonsian attitude. He was kept on the above therapy and discharged from the hospital April 24, 1922. He was kept under biweekly observation for six weeks and there was gradual subsidence of the parkinsonian attitude and gait. He was then allowed to return to his work, and has been constantly at work ever since—in all seventeen months. Examination now reveals no abnormalities except a possible left facial paralysis of peripheral type.

CASE 4.—This patient, aged 30, tailor by trade, entered the hospital Sept. 8 1921. He was very ill, with multiple cranial nerve involvement, and had developed persistent vomiting which caused him to be put on the "most critical" list. For the first four days in the hospital his temperature varied between 98 and 99.6, then suddenly dropped to 97 and for eight days varied between 96 and 97. For the first fifteen days he was given only strychnin nitrate, and on the fifteenth day pituitary extract in addition. At once his temperature began to rise and in eleven days, by steady progression, reached 98; when he was discharged from the hospital, Dec. 6, 1921, it varied between 98 and 98.6. Whereas the vomiting had been a critical symptom prior to the administration of the pituitary extract he vomited only once after its initiation, that being on the second day. From then there was slow but steady subsidence of all symptoms and when discharged he had practically no cranial nerve involvement, but slight residual right hemiplegia. Within a month he was back at work, and has been constantly at work since, a period of twenty months. He now shows no objective findings and has no complaints.

This particular line of treatment was carried out in about ten cases. Those in which it was believed favorable results followed were the acutely ill, the spinal type with marked myoclonia, and the cranial nerve with diplopia type. In the acutely ill and myoclonic types improvement invariably began within from forty-eight to seventy-two hours after the beginning of treatment. In the cranial nerve with diplopia type progress was slower; the cranial nerves showed improvement within a week or ten days and the diplopia disappeared within a month or six weeks. The frankly parkinsonian cases were not influenced at all.

While nothing miraculous is claimed for this therapy, the regularity of the time of appearance and the uniformly similar progress of the improvement was not considered a coincidence, but a consequence of treatment.

II. CASES FROM THE VANDERBILT CLINIC

CASE 1.—*Post-Encephalitic Paralysis Agitans Syndrome, with Unusual Features.* DR. RUBIN A. GERBER (by invitation).

This patient is presented because of the interesting affection of the musculature of the neck causing a movement approaching what has been described as characteristic of dystonia, varying from the usual hyperflexion of the body seen in paralysis agitans by presenting a hyperextension of the head segment.

F. S., a man, aged 20, was first seen Oct. 20, 1923, when he complained of shaking of the left hand and stiffness of the neck. He said that he had had "influenza neuritis" in January, 1920, for three months, the condition being brought on by exposure while shoveling snow. It was characterized by delirium, sharp shooting pains down the left arm, and insomnia for three weeks. This was followed by a period of somnolence of several weeks. For two years, until February, 1923, he considered himself in good health, except for a very slight tremor of the left hand. He worked and had had no other complaints until one day in February, 1923, he was struck by a taxicab. He was dazed, turned white and trembled all over. Apparently he was unhurt, though shocked, and was sent home in a taxicab. That same day he began to notice a violent shaking of the left arm, at times so great as to shake his whole body (the condition he shows at present). Gradually, since then, his head began to be drawn backwards against his will and with difficulty he is forced frequently to flex his head forward. Slowly, involuntarily and gradually the head is retracted again, until there is a disturbance in circulation, the face becoming suffused, the blood vessels of the neck engorged and the muscles strained to the utmost. The mouth remains open and there is marked tremor of the tongue which makes a flapping sound. Mucus and salivary secretion are increased, causing slight choking and drooling. He has observed occasionally slight trembling of the right arm and right foot. Since attending the clinic he has occasionally had "fainting spells" not losing consciousness, but falling to the ground. He becomes blue in the face, froths at the mouth and trembles all over. These attacks last from about five to ten minutes with no incontinence but are followed by marked malaise. Syphilis is denied and the habits are said to be regular. The family history was unimportant.

On examination, he shows markedly abnormal attitudes; marked irregular tremor of the left hand when at rest, which, by its violence, causes the whole arm and left side of the body to shake; flexed attitude of the trunk and extremities though the head is held backwards stiffly. When supine, the feet are extended and somewhat internally rotated. He has a propulsive gait with marked lateropulsion. When standing, he holds the feet together only for a few seconds and then is involuntarily forced to take a step or two backwards to balance himself. There is lack of the associated movements of the left arm and the head when walking, and slighter repression of the associated movements of the right arm. He sits down in one movement—all in a lump. Though there is no definite Romberg sign, he sways considerably and is retropulsed. When sitting for a few minutes, he gradually falls to the left and on one or two occasions has fallen from the chair. There is marked tremor of the left hand when placing finger to nose and also when placing finger to finger. He has slight adiadokokinesis of the left hand and some slight dysmetria. He writes with the typical paralysis agitans incoordination. Speech is dull, weak, and monotonous. Dysarthria is increased by the tongue tremor and excessive mucus production and salivation. There is tremor of the lids and of the lips. The head assumes a hyperflexed attitude by a gradual slow dystonia-like movement.

There are no pathologic reflexes. Muscle strength and muscle status are normal. There are no abnormal associated movements. Nerve status is normal. Sensory examination is negative. The left pupil is slightly larger than the right and both the right and left show slight diminution of the direct light reflex. There are some slight nystagmoid jerks when the patient is lying down and looks to the left. Typical paralysis agitans facies with flattening of both sides of the face, smooth glossy skin and increased salivation are present. The mental status is apparently normal as regards intelligence, memory and attention, but there is marked susceptibility to emotional stimuli. The viscera are normal; pulse 80. Inanition is beginning. Laboratory tests were negative as regards urinalysis, blood Wassermann reaction and spinal puncture.

The several points of particular interest in this case are: (1) The cerebellar phase, with the presence of both intention and volitional tremor, the nystagmus, festination and disturbance of gait; (2) the presence in a case of encephalitis with paralysis agitans syndrome, of a dystonia-like movement limited to the head segment; (3) the relation of trauma, with the incidental emotional upheaval as bearing on the production of the acute phase of the disease.

We might analyze the pathology as a fragmentation of various circuits, showing hyperextension of one segment and flexion in the others. The cerebellum, striate system, static and kinetic mechanisms and perhaps the cerebrum are involved. The latter through pronounced irritation, or the lack of proper inhibition, may be the cause of his fits.

DISCUSSION

Dr. Abrahamson: How long after the accident did the patient note the increase of symptoms?

Dr. Smith Ely Jelliffe: Is there any glycosuria, levulosuria, galactosura, or any blood chemistry change? Have you noticed hyperthermia or changes of the sweating mechanism?

Dr. E. D. Friedman: We have had a similar case at Bellevue. There was hyperextension of the head and sialorrhea. Such cases indicate that there must be segmental innervation in the basal ganglia. All of us who have seen encephalitis will recall cases with focalized rigidity and tremor in one limb or in a particular muscle group. These cases can only be explained by the assumption of segmental innervation mechanisms.

Dr. Gerber (closing): We made only routine examinations of the blood and urine, and these showed nothing abnormal. The only secretory changes are the glossy appearance of the face, the increased salivation and increased mucus production. No hyperthermia has been observed. The increase in symptoms was noticed immediately after the accident.

III. CASES FROM THE NEUROLOGICAL SERVICE OF MONTEFIORE HOSPITAL

Dr. S. Brock: Case 1.—*Unusual Paralysis Agitans Following Acute Epidemic Encephalitis, Showing a Diurnal Variation in Motor Activities.*

A. P., a girl aged 11, was taken ill in February, 1920; abnormal movements appeared which ceased only during sleep. On the third day fever developed and the temperature gradually rose to 104, when she saw double. The next day drowsiness appeared, which increased to lethargy after about five or six days. She was incontinent. The lethargy lasted about six weeks when parkinsonian gait and attitude were noted together with well-marked tremor of the head and

upper extremities; speech became low-pitched and monotonous, until finally, about November, 1921, she became almost entirely inarticulate and swallowing became very difficult.

Physical examination reveals marked parkinsonian rigidity; the head is fixed in a somewhat retracted position and turned to the left; the upper extremities are somewhat adducted at the shoulder, and flexed at the elbows and wrists. The lower extremities are adducted at the hips, slightly flexed at the knees; the right foot is in marked equinovarus position, the left in marked equinus. Everywhere there is "cogwheel" spasticity. She rests recumbent and seems incapable of the slightest voluntary movement. The eyes are turned upward and to the left, the pupils are round, equal and react rather sluggishly to light and in accommodation. Ocular movements are fairly well performed. The fundi are normal. There is the fixed countenance of paralysis agitans with greasy skin. She is unable to protrude the tongue; there is drooling of saliva; swallowing is accomplished with considerable difficulty. In fact, there is a pseudobulbar palsy of striatal type. There is constant coarse rhythmic tremor of the upper and lower extremities which varies in amplitude from time to time. The deep reflexes are quite lively, the right more than the left. There is bilateral ankle clonus, more marked on the left. There is no Babinski sign, and there are no sensory changes. During the day the child lies like a piece of statuary, immobile except for the tremor. At night, usually after dark (9 to 11 p. m.), she arises from bed, walks and is said even to have run about the ward. Speech also is said to have returned in part. These latter manifestations point to a remarkable mutation, which encephalitis has been known to produce in the sphere of sleep. (At Montefiore Hospital, another case of paralysis agitans, following epidemic encephalitis, in a boy aged 17, showed at times a remarkable condition somewhat allied to the above. He would gradually "fold up" in his parkinsonian attitude, falling from an upright position to a crouched, stooped one, and yet when given the command to get up and walk or run, he would do so in a most remarkable manner, which contrasted markedly with the severe paralysis agitans present.) The examination of blood, spinal fluid and urine gave entirely negative results.

Case 2.—S. G., a man aged 42, with past history irrelevant, became ill in 1920 with headaches, double vision, marked insomnia, and fever. He "recovered" and returned to work. One year ago he noticed that he could not work as fast as formerly and that there was a certain stiffness and pain in the back. Six months ago he began to complain of tremor in his hands and, to a lesser extent, in his feet.

Physical examination reveals a typical parkinsonian facies. The gait is normal, except for the loss of associated swing of the upper extremities which are held in the typical parkinsonian posture. There are: slight blurring of the left fundus, slight left ptosis, wide palpebral fissures, prominent eyeballs, and definite bilateral von Graefe sign. The movements of the eyes show "cogwheel" phenomena. There is weakness of both external recti muscles, and the eyes can converge scarcely at all. The pupils are equal and react fairly well to light and in accomodation. The left side of the face is slightly paretic. The tongue protrudes slightly toward the right and is somewhat tremulous. The left side of the palate seems to hang lower than the right.

There is a curious smacking movement of the lips, associated with which is a swallowing reflex. This movement occurs at the rate of about five to ten a minute. It ceases when the eyelids are closed and also on command. The patient volunteers the statement that he performs this movement because of dryness of mouth and tongue. There is marked rhythmic tremor of the hand.

While the deep reflexes are generally increased there is no clonus or Babinski sign; the superficial reflexes are very lively. There are no sensory disturbances. The face shows a greasy skin; the mouth does not show undue dryness.

DISCUSSION

DR. STEPHENSON: Has she had any form of treatment?

DR. BROCK: She has had nonspecific protein therapy. She is to receive typhoid vaccine.

DR. RILEY: Can you describe the circumstances under which she regains voluntary control?

DR. BROCK: I have not witnessed this myself but the interns have seen it frequently

DR. ABRAHAMSON: This case is one of the group I reported at the Boston meeting of the American Neurological Association. The phenomena and causation of the phasic and permanent mutations in lethargic encephalitis were discussed and analyzed. The frequent nocturnal mutations are of special interest; this conversion of the activities of the day into those of the night and vice versa have been noted by many observers. Mutations for a time phasic may eventually resolve themselves into permanent conditions. Syndromes with all appearances of permanence may remit and remain absent for an indefinite time; or a different syndrome may appear on the next occasion. In the phasic alterations we must predicate the intactness of the upper and lower motor neurons. The will to move is affected; the central organ of tone suffers. It is a serious mistake to regard these patients as hysterical, or worse, as malingerers.

DR. HENRY A. RILEY: Is there any synchronism in the movements between the right upper extremity and the left lower extremity? It appears as if there were. This would be interesting in relation to the crossed motor association seen in quadrupeds between the right fore foot and left hind foot, and vice versa.

DR. J. H. LEINER: Does this child speak at night? One little girl kept up continuous talking from 8 p. m. to 5 a. m. It was practically a monosyllabic repetition of: "Mummy, are you asleep? Daddy, are you asleep? I'm going to sleep," over and over again. The parents thought it was hysterical and tried to break her of it by punishing her. They could not stop her. This child now presents a typical postencephalitic parkinsonian condition. She has gained 50 pounds (23 kg.) in weight.

DR. BROCK: I am told this girl articulates at night, but in the day time it is impossible for her to talk.

DR. SMITH ELY JELLIFFE: Some may recall Vogt's interesting discussion of the striatum syndromes, and particular attention may be directed to his thesis in the Heidelberg Akademie der Wissenschaften, 1919, in which he emphasized the value of an understanding of the striatum regions as a possible structural substrate of many emotional reactions. Hysteria was particularly mentioned. Kappers' recent study of the phylogeny of the striatum in birds and the relations of these to that region in man has advanced the question a step further. He has made it more clearly appreciable that some day we may be able to talk of the "anatomy of the unconscious," i. e., the fiber connections that hitch up the older affective processes to the vegetative life of the "organism as a whole." In this study he more closely points out the fact that the "paleostriatum" in some of its nuclear and fiber arrangements is to be considered as an outgrowth, not of the diencephalon, but of the telencephalon or cortex. Here may be traced the

anatomic ways through which the cortex, through so-called physical function, is intimately bound up with the vegetative or affective craving portions of the body. So much for anatomic considerations. As for the psychologic situation, we are all familiar with Janet's older generalization concerning the "lowering of tension of the psychic level." This is what happens with this type of case, speaking in a general manner. War experience showed this, and a great number of experiments bear on the issue. These may result, either from direct injury, inflammations, emotional shock, toxemias, etc.; the cortical *balancing factors* are removed and the primary vegetative factors come to the surface. Then, during the night time, or under any influence that narrows the issues to primary stimulus, the cortical regulating factor on the disordered motor mechanism is partially reestablished. Thus these patients are apparently well at night, or they can dance or sing in response to the stimulus of a graphophone, a piano, a funny story, or anything that releases a simple emotional response. The paleostriatal motor coordination pathways are for the time surcharged with affective tension, get to the cortex via the pathways indicated, the which are only partially destroyed structurally, and the peculiar motor manifestations, or mutations, as Dr. Abrahamson terms them, are modified, or disappear. I would call your attention here to Verger and Hesnard's (*Journal de médecine de Bordeaux*, Sept. 25, 1922), Pette's (*Deutsche Zeitschrift für Nervenheilkunde* **76**: parts 1-4, 1923), Salmon's (*Riforma medica* **39**: No. 6, 1923), and Lewy's (Tonus und Bewegung, Berlin, Julius Springer, 1923) studies in this connection, where these brady-kinetic phenomena are exhaustively considered, not to mention many others already cited in the last edition of Jelliffe and White's "Diseases of the Nervous System," 1923.

DR. BROCK: This patient is able to stop the movements of the mouth when given the command.

DR. ABRAHAMSON: That means really that it is an early stage. Later he will not be able to respond to command. He will lose control.

DR. CRAIG: It would be interesting to see if he can still move the mouth when keeping his eyes closed.

DR. SMITH ELY JELLIFFE: I wish to emphasize what Dr. Abrahamson has said. His point is extremely interesting. This whole series of phenomena reminds us that we have been too much inclined to regard the human being as a machine working by itself of itself, and have forgotten how far it is related to the environmental stimuli. We must regard the individual as a transforming mechanism. The environment is always playing on the individual. In the average physiologic state we are able to handle the stimuli. The phenomena not only involve the associated movements, but the cutting out of stimuli that are always falling on the nervous system force a new state of adjustment. A diaschisis results (v. Monakow). In these patients stimuli are cut out because the organism is not able to handle them. If you can remove the stimuli that overcome them, the phenomena disappear. This may be a mechanism of defence, as the turning off of the stimuli may help the organism to regain its equilibrium.

DR. JOSHUA H. LEINER: The question of therapy in epidemic encephalitis arose this evening. During the early days of the epidemic in this country a belief arose that thecal puncture improved the patient. This view was short lived. Very little if any therapy was resorted to at this time. Later, reports began to come from Europe (chiefly from France) that nonspecific therapy was in use. Marinesco used serum intraspinally, Döllkin used milk. Brill in this country was using serum intraspinally. A well known bacteriologist from a

western institution has been using horse serum which he believes is specific. Its use in two of my cases was followed by severe anaphylaxis, one case showing alarming crises, vagal in type. She died a week later. Judging from the favorable reports that emanate from this investigator, it is my conviction that his good results are in the main due to nonspecific proteins within the serum.

Three years ago I used turpentine for the production of a fixed abscess in a woman who was in a lethargic state for five weeks in St. Mark's hospital and three weeks on our neurologic service in Lebanon Hospital. She was losing very rapidly. Her vasomotor system was failing, and her blood pressure dropped to an alarming level. Her condition being very precarious and as a last resort we produced a fixed abscess. The change was most dramatic. In three days her eyes were wide open, and in nine days she was on a wheel chair. She was then sent to the Montefiore Hospital to convalesce and is now well. The production of antibodies due to a fixed abscess, which is an old remedy, improved this woman.

A case of epidemic encephalitis in a child showing sequelae of respiratory and conduct disorders (*Journal of the American Medical Association* **81**:1284 [Oct. 13] 1923) got better spontaneously following an attack of lobar pneumonia. The production of antibodies on the basis of nonspecific reaction improved this child.

As a result of these observations I began to treat my patients on the basis of nonspecific therapy, using a nonspecific protein in the form of sodium nucleinate (Merck). With a preparation of this type of protein we have the advantage of graduating the dose, and thereby control the phase of anaphylaxis. Then again, its pharmacologic and physiologic properties are well known, even preceding Netter's use for the parasyphilitic diseases, i. e., the production of leukocytosis and phagocytosis.

I have used this now in over twenty-five cases with very favorable results. Nineteen of these cases were in the acute-subacute stage of the disease. This nonselected group were all severe cases entering the wards of Lebanon Hospital. One fatality took place, and this was in a case in which treatment was first started three weeks after the onset. In the acute stage we begin with a half grain subcutaneously, watching the reaction, i. e., temperature, pulse, total and differential white count. In the subacute, chronic variety, when a fixed pathology is already present, one can hardly expect much, but may attempt to stay the progress of the disease.

In this disease there is no frank reaction on the part of the organism, as is evidenced by the lack of leukocytosis, with its oft accompanying phagocytosis. Spiller and Ayer have made note of this fact, i. e., the lack of leukocytosis. A reaction of the host to an invading organism, creating the production of antibodies is an all important item in an infection. Our specifics, such as arsphenamin and quinin, have the property of producing leukocytosis. In the early days when intravenous arsphenamin was combined with subcutaneous injections, the Wassermann reaction disappeared much earlier, this being due to the greater leukocytosis. The use of quinin in puerperal infections is given for the same reason. Wagner-Jauregg's treatment of general paralysis is nonspecific therapy.

I am frank to say that I do not know what my results will be in years from now. I know of two severe cases that I have had under observation for nearly two years, one a hard-working U. S. mail carrier, who is out in all weathers, and performing his usual duties. The other was a patient of the late Dr. Leszynsky, whose condition was so desperate at the time that he felt very little harm could be done if this new therapy was given. He had a very severe reaction, after

the first dose, but recovered, and is now working as a tailor. In regard to the good results following the use of pituitary extract, as shown by Dr. Stephenson, I believe the effect is due to a protein. When strychnin nitrate was given alone, there was no improvement, but given with increasing doses of pituitary extract, there was improvement. I believe this is a nonspecific result.

I think we ought to try and do something for these patients, instead of leaving them alone until a specific remedy arises. We should use our armentarium as physicians, and do what good we can. Surely no harm can come from the above procedure.

Dr. E. D. Friedman: The encephalitis epidemic has taught us the important rôle which the basal ganglia play in the genesis of abnormal involuntary movements. These great structures are no longer the *terra incognita* of the brain. Prior to the encephalitis epidemic, many of the bizarre movements which could not be explained were labelled hysteria. We now know that most of them have an organic basis. Observation and study of the postencephalitic sequelae have confirmed the work begun by the Vogts and Foerster in Germany, and carried on in this country by Hunt, on the extrapyramidal syndrome. We now know that most of the parkinsonian syndromes are due to lesions in the globus pallidus, and that the putamen-caudate or striatum proper is the site of the pathologic process in cases presenting choreiform and athetoid movements. Probably the dystonias also belong in this group. The substantia nigra has come prominently to the fore in recent pathologic studies.

The encephalitis epidemic has taught us further the importance of the midbrain as the great vegetative center. The lethargy and sleep disturbances noted in encephalitis, both during the course of the disease and as sequelae, confirm the theory of Troemer, who postulated a sleep center in the midbrain. It is disturbance in function of this center which leads to stupor in polioencephalitis superior (Wernicke). The profuse sweating, the greasy face, due to increased secretion of sebum, the disturbances in metabolism, often leading to marked increase in weight, the sialorrhea, the frequency of bladder symptoms, particularly in the acute stage of the disease, the respiratory disturbances noted often during the later period, and the presence of tachycardia in many of the cases in spite of the relatively low temperature—all emphasize the significance of the midbrain and hypothalamic region as the center of our vegetative life.

Dr. Abrahamson: The cases presented bring up two very important problems: one, the relationship between accident or trauma and encephalitis. There is no doubt in my mind that accidents can later accentuate or initiate recurrences or exacerbations of lethargic encephalitis; it acts as an activator or accelerator of the morbid process; its effects are physical or psychic, especially emotional. The second point of interest relates to marriage and lethargic encephalitis. This subject must be met squarely; considerable unhappiness has resulted from the marriage of patients who have had lethargic encephalitis, and who, for the time being, present little or no evidences of the disease. No one is in a position to predict when or in what fashion the disease may reappear as a chronic manifestation, neither can we tell any patient that a recrudescence is out of the question. The specific action of the virus on the basal ganglia and the frequency of disturbances of the sexual sphere, along with the mental manifestations, all must make us very cautious in recommending marriage. The clinical resemblances between lethargic encephalitis and epidemic poliomyelitis must be borne in mind. The present rather mild, though fairly extensive epidemic of poliomyelitis, has presented many cases in which a clinical differential diagnosis was well nigh impossible; the determining factor being that one was

prevalent and the other was not. As regards therapy: in the acute and subacute stages from 80 to 90 per cent. recover from the acute illness, apparently independently of therapy. Once the chronic manifestations, such as parkinsonian or dystonia syndromes exist, little can be hoped from nonspecific or any form of treatment. Efforts should be directed with nonspecific therapy to prevent, if possible, the occurrence of chronic manifestations—therapy that has been under way for the past three years.

MAJOR JARVIS (by invitation): What is the mortality over a number of years? I was reading a report of deaths in the last year and did not see any deaths listed from encephalitis.

DR. GROSSMAN: That is a difficult question to answer for any given year. Following the mortality over a number of years in the various epidemics, it is found greater in some than others. In a group of 145 cases observed at the Mount Sinai Hospital, over a three year period, it is 20 per cent. I think that is actually too high because the cases were of a severe type. The average mortality would be nearer ten than twenty if another group of cases were studied.

DR. STEPHENSON: In hospital statistics the mortality among adults is 10 per cent. and among children 15 per cent.

DR. SMITH ELY JELLIFFE: It is necessary to go beyond the narrower nosologic considerations raised in a slightly overacademic manner by Dr. Abrahamson. He has spoken of the needs of closer clinical differentiation between what we have been pleased to call encephalitis, and what we have been pleased to call poliomyelitis. These may not, after all, be separable. If we go into the history of epidemics we might raise a question as to what we have been pleased to call influenza. From the fourteenth century on we have historical documents showing the presence of all these kinds of clinical medleys associated with influenza. By what differentiation are we entitled to say that these psychotic, neurologic, psychologic symptoms are due to influenzal poison, to encephalitis poison, or to poliomyelitic poison? There may be shifting types of reactions in the nervous system to a mixed virus which may be expected according to the degree of stress in which the individuals are involved. Here environmental factors of an important nature may have to be included. This is not merely my own hypothesis. Lépine of Lyons, at the Paris Congress of 1921, and others have raised the same issue, and have emphasized the possibility that the more intense types of reaction involving vegetative levels of life and which gave rise to what we are now calling encephalitis lethargica, might be better understood when the enormous economic stress throughout the entire world, the population being involved in much more acute conditions having influence on the vegetative life, were considered. The virus therefore produced the type of disease we call encephalitis lethargica, because the vital affective pathway portions of the nervous system were under greater stress. The factor of predisposition of localization of a disease process, causing different clinical pictures, by reason of different environmental stresses became germane to the discussion. I have not infrequently called attention to this in the various syphilitic processes. In former years great discussions arose as to the differentiation of different diseases of the nervous system, which were all shown to follow one virus, syphilis. But why the process should be a general paralysis, a gastric crisis, a myelitis, that had to be relegated to other more obscure factors in the discussion of which the definite stresses of the affected organs needed to be incorporated. I have frequently mentioned the possibility of a rectal tabetic crisis being a resultant first of the syphilitic virus, but secondly located where it is because of a psychanalytically understood perverse anal eroticism.

PHILADELPHIA NEUROLOGICAL SOCIETY

Regular Meeting, Nov. 23, 1923

C. M. Byrnes, M.D., *President, in the Chair*

A CASE OF TABES DORSALIS SHOWING AN ACTIVE IRITIS. Dr. E. H. Erney.

A white man, aged 62 years, a piano mover, with an unimportant family history, was taken ill about two years ago with pain in the back and left leg, followed by shooting pains in both legs. One year later he noticed unsteadiness in his gait. The eye condition began in July, 1923, with intense pains in the left eyeball and left side of the face, associated with photophobia and marked redness of the eye. The patient had been married twenty-one years; there were no children, and the wife had had no miscarriages. He denies venereal disease and says that he has always been healthy until the present illness. He never drank until he was 45 years of age. Forty years ago he was struck in the left eye with a piece of steel which was removed, after which he made a prompt recovery.

Examination showed a badly inflamed and painful left eye with blindness; both pupils were immobile and the ordinary signs of tabes were present. The Wassermann reaction was strongly positive. We treated him with potassium iodid and mercury almost to salivation but with no improvement in the eye symptoms, nor in his general condition. Later we gave him a course of arsphenamin. After three injections the improvement in the eye condition was striking—the congestion was greatly improved, the photophobia was lessened and he felt generally much better.

There are two conditions in this case of interest: first, whether the iritis was due to syphilis, and second, the relative merits of various forms of antisyphilitic treatment.

Referring to the second question, I have investigated this matter in order to present it in some concrete form. I quote from Dr. Jos. V. Klauder, who states: "while there is no definite proof, syphilographers have formulated a ratio, which they feel is fairly accurate in representing the relative efficacy of certain drugs in the treatment of syphilis. They place arsphenamin at 10, bismuth salts at 8, and mercury at 4."

DISCUSSION

Dr. H. Maxwell Langdon: The point of interest from the ophthalmologic standpoint is whether the iritis is due to spirochetal infection, or to some other etiologic factor. There is no question that the man has syphilis, and that he has iritis. I doubt whether the two can be associated. In the first place, specific iritis is usually bilateral. In this patient it is unilateral. Specific iritis usually occurs during the secondary stage, this, if it has resulted from syphilis, in the late tertiary stage. That is most unusual. Specific iritis does not usually involve the cornea, nor produce so much congestion of the iris in only one portion. In this case there was blood in the anterior chamber. The cases of iritis which have so much engorgement of the iris—I have seen one with the anterior chamber so filled with blood that nothing would control it except leeches—are usually of focal infectious origin. The left eye as it appears now is almost typically that which results from either sphenoidal or ethmoidal disease—a condition that has not been excluded in this case. Against this and for the spirochetal origin is the fact that when arsphenamin was admin-

istered the ocular condition improved. It is possible that in some way intranasal drainage was established and the sinus condition quieted down. At present the lower part of the cornea is distinctly involved, which is the part more frequently involved in sinus conditions. My own feeling is that the iritis is not spirochetal in origin, but is due to ethmoid or sphenoid disease. If we could get accurate statistics on iritis at the present time, the part which specific infection plays would be 8 or 10 per cent. I believe 50 per cent. of iritis is due to focal infection. I know of three cases of chronic appendicitis that produced iritis. Another factor in lessening the production of iritis is that syphilis is so much better treated than it was ten years ago. .

A CASE OF AMYOTROPHIC LATERAL SCLEROSIS OF RAPID DEVELOPMENT IN A GIRL OF TWENTY-SIX. Dr. Louis O'Brasky.

The patient, a white domestic, 27 years of age, was well until July, 1922, when she noticed her right hand becoming weak, the weakness increasing progressively; although it extended up the arm she continued to work. In October, 1922, she found that the fingers of this hand became permanently flexed and she was unable voluntarily to open her hand. She had no pain, but the hand would become stiff, especially in cold weather, and she complained of vague gastric disturbances. In February, 1923, she was referred to the Orthopedic Hospital where she was studied for three months. In June, 1923, the weakness extended to the right leg, followed shortly by weakness in the left leg. She was admitted to the Philadelphia General Hospital in August, 1923, complaining of loss of power in both upper extremities and difficulty in walking. The right hand had become so weak that she was unable to comb her hair and she could raise the arm only with difficulty. She was conscious of twitching of the muscles of the shoulder.

A month before admission she noticed difficulty in swallowing and pronounced difficulty in talking. Her lips seemed to be stiff. These symptoms are becoming worse gradually.

There is a family history of tuberculosis and of cardiorenal disease. No member of the immediate or remote family had a disease resembling hers. She has never had a venereal disease.

The general physical examination reveals a tuberculous infiltration in the left lung. The cranial nerves are negative except for fibrillary contractions in the tongue, weakness in the pharyngeal muscles and difficulty in approximating the vocal cords. All reflexes are markedly exaggerated with bilateral Babinski sign, patellar and ankle clonus. Atrophy of muscles of both upper extremities is present and advanced. Fibrillary contractions are noticed in muscles of the shoulder girdles. The power of all extremities is affected, but more on the right. Spasticity is noticed in all four extremities, more marked on the right side. She presents no sensory symptoms, and all laboratory reports are negative. She had been given doses of arsphenamin at the Orthopedic Hospital which made her sick.

This case is presented for two reasons: the early age of onset (26) and the rapidity of the course.

DISCUSSION

Dr. A. J. Ostheimer: I think I am correct in saying that there was no mention of the pupillary reaction to light, nor of any examination to determine the presence of aortitis or of leukoplakia. Léri has recently laid stress on these three clinical signs of syphilis, which frequently are present even in the

absence of a positive Wassermann reaction in the blood or spinal fluid, and even in the absence of both clinical symptoms and laboratory findings the advisability of antisyphilitic treatment should be carefully considered in such a case.

DR. ALFRED GORDON: About eight or nine years ago I presented a boy, aged about 17 or 18, who had an attack of acute anterior poliomyelitis from which he partially recovered. He sustained a trauma and then began to develop symptoms of amyotrophic lateral sclerosis.

DR. WILLIAM G. SPILLER: One of the most interesting features of this case is the age at which the disease developed, 26 years. In writing a chapter for Osler and McCrae's "Modern Medicine" I investigated the age of onset for amyotrophic lateral sclerosis and quote now from my chapter. Marie gives the onset as occurring between the ages of 35 and 50 years; Dejerine, the second half of adult life; Oppenheim, middle life; Eichorst, between 35 and 50 years; Gowers, between 25 and 45 years; Strümpell, between 25 and 40 years. In Probst's statistics of forty-seven cases the disease began most frequently between 30 and 50 years, in thirteen cases between 50 and 60 years, in five cases between 60 and 70 years, and in one case after 70. Rossi and Roussy conclude that the beginning is usually between 30 and 50, although frequently between 50 and 60 years; it is rare between 60 and 70, and exceptional after 70 years.

MYOTONIA ATROPHICA. DR. T. H. WEISENBURG.

The case presented is of interest because of the infrequency of the disease, its long duration and the endocrine aspect. The patient, 38 years of age, a cutlery grinder, shows in his family history consanguinity—one maternal cousin with paraplegia, one with "shaking palsy," and a maternal grandfather with senile tremor.

At the age of 17, the patient's right hand became slightly stiff and there was difficulty in opening it when closed. At the same time there developed twitching movements in the muscles of the right upper arm. Three years later the same condition occurred in the left upper extremity. The progress of the disease was gradual. In the last ten years twitchings have occurred in the shoulders, thighs and legs. Five years ago the neck, tongue and jaws became slightly stiffened and it was difficult to relax them. Speech became slightly difficult. Three years ago weakness developed in the legs and feet and a swaying motion of the body when sitting or standing erect. There has been slight difficulty in swallowing food. Recently progress has been much more rapid so that it is difficult for the patient to follow his occupation. The past medical history is unimportant.

Examination reveals atrophy of the muscles of the face, neck, forearms, legs and feet. Fibrillary twitchings are observed throughout the entire body. There is a to-and-fro swaying of the body, when standing or sitting, usually from side to side. The strength of the hand grips is markedly decreased. The muscles of the forearms and hands fatigue rapidly. The biceps and triceps reflexes are decreased and the knee jerks are greatly diminished. The left achilles jerk is absent and the right barely present. The abdominal, cremasteric and plantar responses are prompt. The muscles of the upper arms and thighs are not powerful or well developed. There is no cataract. The teeth are in good condition, but the tonsils show a chronic infection. Visceral examination is negative.

The blood count shows 40 per cent. lymphocytosis. Glucose tolerance shows a rather high and sustained curve. There is marked sensitiveness to epinephrin and pilocarpin, but little reaction to atropin. Basal metabolism test is minus 30. The serologic tests are entirely negative .

This case fits in well with the descriptions of myotonia atrophica by W. J. Adie and J. G. Greenfield (*Brain* **46**:73 [May] 1923). Tremors were very numerous in this case. Cataract occurs in about 30 per cent. or more of these cases but is absent in this patient. There is no testicular atrophy, but marked loss of sexual power. Loss of hair and scanty hair distribution, sweating and acrocyanosis are common manifestations and are found in this patient. Adie and Greenfield mention a marked familial tendency, but I was unable to demonstrate it. The low basal metabolic reading and the high lymphocyte count suggest a definite thyroid relationship to the disease. There certainly is a metabolic disturbance. The question of anterior horn cell disease, to account for the fibrillary twitchings in this case cannot be answered at present.

DISCUSSION

DR. H. MAXWELL LANGDON: The lenses were perfectly clear when I examined the man recently at the Orthopedic Hospital.

DR. ALFRED GORDON: Were the mechanical or electrical reactions typically myotonic and were they confined to the atrophied muscles?

DR. CLARENCE A. PATTEN: In reply to Dr. Gordon's question, I believe that most of these cases show a mechanical irritability of the muscles throughout the entire body; the atrophy, however, is not universal, at least in the early part of the disease. It is rather interesting from the endocrine viewpoint that after three weeks of pituitary and thyroid feeding, there has been a disappearance of fibrillation of all the muscle groups of the body, except the left arm and forearm; whether it is a coincidence is a question. We have as a basis for therapy, a very low basal metabolism and a physical habitus which indicates a thyroid condition. Dr. Burr asked about cataract, the man has had no cataract and there is no history of cataract in the family so far as we know.

A CASE OF HEMIATROPHY OF THE TONGUE. DR. F. H. LEAVITT.

This patient is presented to the society because of a marked hemiatrophy of the tongue. He also complains of headache and vertigo, associated at times with vomiting. He has weakness and awkwardness in the use of the right arm and a subjective sense of numbness of the right side of the face, and on the right shoulder and arm. Occasionally he has noticed regurgitation of fluids through his nose. He worked on a vaudeville circuit as a dancer until induction into military service. He had scarlet fever and diphtheria when a child but denies venereal infection. He states that his nervous symptoms date from July, 1918, when he was buried in a trench by shell fire. Following this concussion, he noticed fatigue on slight exertion, headache and vertigo, which is most noticeable when he exercises or moves his head from a vertical plane. Sept. 27, 1918, he was wounded in the left leg by a machine gun bullet. Because of this injury he has had a recurrent osteomyelitis of the left tibia, for which he was operated on in July, 1922. In the winter of 1920 he had lobar pneumonia. In 1919, he first noticed awkwardness and aching in the right arm and a sense of numbness over the right side of the face. He next noticed that he had difficulty in controlling the finer movements of the right hand and dropped

things from that hand. In 1920, a physician at the U. S. Veterans' Bureau discovered the present condition of the man's tongue, namely a wasting and "wrinkling" and wormlike movement of the right side. At times the patient felt as though there were too much saliva in his mouth and he had difficulty in swallowing it. During the past year his headaches have become more severe, are pronounced in the right frontal region and have been associated with nausea. During the past few months he has noticed an increasing dimness of vision of the right eye.

The patient is a well nourished and developed young man. He has atrophy, with wormlike fibrillations, of the right side of the tongue, with some loss of tactile sensation on the affected side of the tongue. Taste and smell are unimpaired. Vision in the right eye is 5/12, in the left eye, 5/5. The palpebral fissures are equal, the lid motions normal and the extra-ocular motions full and equal. The right pupil reacts sluggishly to light, the left gives a better response to light; the pupils are equal. The media are clear; both disks are atrophic, pale and with sharply defined margins. Dr. H. M. Langdon diagnosed the condition as optic atrophy, particularly marked on the right side, probably primary. Paresis of the right side of the face is present. Hearing is normal and the Bárány tests are normal. The left side of the palate is weaker than the right, but there is much scar tissue present, following a tonsillectomy.

There is diminution of tactile sensibility in front of both ears. There is hypesthesia in the lower part of the right side of the face, on the right side of the neck and on the right shoulder. Pain and temperature (heat particularly) sensibilities are lost over the entire right side of the face, neck and shoulder. There is a similar area on the left side but not quite so complete or widespread.

The man has no real paralysis in any movements of the right hand despite the fact that he complains of lack of control in this member. The patellar and achilles reflexes are increased but equally so. Plantar stimulation produces dorsal extension on each side of all toes. Clonus and spasticity are not present.

Electrical examination shows no changes in quality or quantity reactions in any muscles of arms, face and neck. The roentgenogram of the skull, the blood Wassermann reaction, blood count, urinalysis, and spinal fluid are normal in every respect.

A review of the literature reveals comparatively little concerning this condition. Burr (*Journal of Nervous and Mental Diseases* **23**:458, 1896) reported a case before the Philadelphia Neurological Society in April, 1896, the patient presenting symptoms similar to those observed in this case. The patient gave a history of syphilis, and Dr. Burr was inclined to believe that there was a syphilitic meningitis affecting the base of the brain and compressing the nerves. In Burr's article, mention is made also of cases reported due to tumors in or near the medulla. Hemiatrophy of the tongue has also been reported as occurring in cases of syringobulbia. Leudit (*Annales des maladies de l'oreille* **13**:614, 1887) reported two cases due to specific softening of the nucleus of the twelfth nerve. Schiffer (*Revue mensuelle de laryngologie* **1**:377, 1886) reported a case following gunshot wound of the occiput. Von Limbeck (*Prager medizinische Wochenschrift*, 1889, p. 181) reported a case of hemiatrophy of the tongue with fibrillary twitchings occurring acutely, following a cellulitis of the arm. Pel (*Berliner klinische Wochenscrift*, 1887, p. 521) reported a case which he considered to be syphilitic arteritis affecting the nuclei of the tenth, eleventh and twelfth nerves. Postmortem examinations of cases of hemiatrophy of the tongue have revealed many different pathologic conditions. When it occurs in the course of tabes dorsalis there is always nuclear disease. Dupuytren (*Clinique chirurgical* **1**:403

and **3**:364) reported a case due to compression of the hypoglossal nerve by an hydatid cyst. Tumors of the medulla and of the surrounding contiguous parts have been discovered to be the causative factors in several cases. W. J. Taylor reported a case due to an infiltrating unilateral tumor of the medulla.

Burr concluded that when there is hemiatrophy of the tongue, with no symptoms referable to other nerves, the lesion is in the hypoglossal nerve itself. In conjunction with symptoms referable to other nerves, it is not necessarily proved that the lesion is within the medulla. Fibrillary twitching is much more apt to be found in nuclear disease than in neuritis. To quote Burr:

"The lesions found postmortem vary greatly. There may be chronic nuclear degeneration (especially in association with diseases of the spinal cord). The results of embolism, thrombosis, or hemorrhage, a tumor arising within the medulla and confined to one side, a tumor growing from the membranes or bone, meningitis, caries, hydatid cysts, or direct injury from wounds. It is probably more frequently associated with locomotor ataxia than with any other disease of the spinal cord, but it may occur in syringomyelia and in the spinal type of general paralysis. In bulbar paralysis, the atrophy like the other symptoms is practically always bilateral. The most common clinical picture is hemiatrophy with palsy of the palate and larynx on the same side accompanied by fibrillary twitching. Very often there is persistent head pain in the occiput on the corresponding side, and this seems to be more apt to occur and to be more severe in cases in which the lesion is not within the medulla, and hence is of some slight value in making the diagnosis of locality. The ocular symptoms which sometimes occur, are a complication due either to an independent nuclear lesion or the extension of a meningitis, say, rather than a part of the natural course of the affection.

"The most frequent predisposing cause probably is syphilis. It probably will be proven in the future that the poisons of the acute infectious fevers, as for example, scarlet fever, are occasional factors in causation."

DISCUSSION

Dr. George Wilson: Dr. Leavitt's case is probably one of neurosyphilis manifesting itself chiefly as a basilar meningitis, although the possibility of a nuclear involvement should be borne in mind. The fact that the man has optic atrophy points to a wide spread condition rather than one localized in the medulla. Negative spinal fluid and blood examinations are occasionally seen in long standing syphilis of the nervous system; these negative results may be due to treatment. I believe it is far fetched to conclude that the present symptoms are in any way dependent on the concussion which he says he suffered in July, 1918.

Dr. A. J. Ostheimer: This case might be one of muscular atrophy of spinal origin, and therefore syphilitic. In this case the nuclei in the bulb—certainly that of the twelfth nerve and perhaps also that of the fifth—were affected primarily, with the possibility of other bulbar nuclei and the anterior horns of the spinal segments becoming diseased later on, resembling certain cases of amyotrophic lateral sclerosis. The optic nerve condition adds to the probability of a diagnosis of neurosyphilis.

Dr. N. W. Winkelman: I cannot agree with the pathologic anatomy as given; I consider marked fibrillary tremors as the result of a nuclear lesion. In this case the twelfth nucleus on the one side is involved. The dissociation of sensation, as shown by the marked involvement of pain and temperature, and very slight of touch limited to the upper extremity, neck and face would,

to my mind, place the lesion within the upper cord and lower medulla, rather than without. Optic nerve atrophy has been reported in similar conditions by Weisenburg and Thorington who explained it on the basis of a resulting internal hydrocephalus. I do not see how we can stamp this man as syphilitic. My diagnosis would be syringobulbia, which might have had its inception as a result of hemorrhage at the time when he sustained his severe concussion.

Dr. Daniel J. McCarthy: For years I had under observation a man with epilepsy, and the only symptom of organic nervous disturbance was hemiatrophy of the tongue with marked fibrillation. He had occasional epileptic attacks, but often would have no attack for months. Notwithstanding negative serologic findings, I always believed that he was a case of inherited or acquired syphilis.

Dr. F. H. Leavitt: As Dr. Burr has said, it seems unwise to make a definite diagnosis, although one may advance many theories as to the pathology. I was of the opinion that this man had an intramedullary condition following the concussion he had in France, after which the present symptoms began.

TWO CASES OF ACUTE EPIDEMIC ENCEPHALITIS OCCURRING IN THE SAME FAMILY.

Dr. Franklin G. Ebaugh.

Since the appearance of epidemic encephalitis, many articles have been written regarding the question of contagion in this protean disease. Netter (*Bulletin de l'academie de médecine* **83**:373 [April 27] 1920), Stern (Berlin, Julius Springer, 1922), Flexner (*Journal of the American Medical Association* **74**:865 [March 27] 1920), Stiefler (*Zeitschrift für die gesamte Neurologie und Psychiatrie* **24**:396, 1922), Wechsler (*Neurological Bulletin* **3**:87 [March] 1921), Guillian and Lechelle (*Bulletin de l'academie de médecine* **84**:321 [Dec. 14] 1920), Laroche (*Paris médicale* **10**:383 [Nov. 13] 1920), Levy (*Bulletin et mémoires de la Société médicale des hôpitaux de Paris* **44**:1007 [July 9] 1920), Fyfe (*Lancet* **1**:379 [Feb. 24] 1923), Lemerre (*Bulletin et mémoires de la Société médicale des hôpitaux de Paris* **44**:1628 [Dec. 31] 1920), and recently Hunt (*Journal of the American Medical Association* **81**:16 [Oct. 20] 1923) in a report of the 1923 New York epidemic, have contributed case reports to the literature or have summarized a large number of cases in which the elements of contagion is freely discussed. This question is an important one in the hospital management of the disease. The object of this paper is to report two cases of acute epidemic encephalitis occurring in the same family. The fact that both of these cases developed under poor hygienic conditions, in which a family of five were living in the same room, must be considered. All five members of the family were affected with an influenzal condition approximately at the same time.

REPORT OF CASES

Case 1.—A girl, 13 years of age, in whom the onset of the present attack was in November, 1919, with symptoms of a respiratory infection, marked asthenia, many aches and pains about her body and occasional vomiting. She was said to have had a cold in her head, also slight fever. On the second day her mother noticed that her eyes were crossed, and the child complained of double vision. During the next week she was apprehensive and had visual hallucinations. She was in bed during this period of approximately two weeks. She was never lethargic, but developed a marked insomnia with agitation at night. On getting up two weeks after the onset of the illness the patient developed choreiform movements for which she had been treated for the past few years in various dispensaries.

On the advice of a physician she later had a tonsillectomy. In 1920, when she first reported to our neuropsychiatric clinic, routine physical examination revealed mitral stenosis. At this time she showed typical generalized choreiform movements and was quite agitated. She was sent for a rest period in the country, where she remained for several months until the choreiform movements disappeared. Neurologic examination revealed weakness of the left external rectus, unilateral ptosis and marked incoordination in the finger-to-nose test. On several occasions she showed slight nystagmoid movements.

Secondary sex characteristics since puberty have been markedly established. She has been growing obese but has shown no behavior abnormalities in school where her progress has been normal. At home she is irritable, fussy, obstinate, sullen and quarrelsome. No definite delinquent acts have been noted and behavior abnormalities for the most part have played an insignificant part as a sequel of the disease. During the last visit to the clinic, she showed no evidence of incoordination of any description and apparently has been adjusting herself well.

Spinal fluid and blood examinations, when she was admitted to the hospital, were negative.

Case 2.—A girl, 11 years of age, a sister of the patient in Case 1, with whom she slept, was taken sick with practically identical symptoms a few days after her sister, her chief complaints being headache and dizziness. Her eyes were crossed and she had diplopia, and she has had persistent strabismus since. For brief periods she was delirious at night, reacting on several occasions to visual hallucinations. There have been no sequelae of neuropsychiatric significance with the exception of the strabismus. She has been progressing normally in school. Laboratory examinations were negative.

The mother had a very severe attack of influenza, with the findings of acute respiratory infection and delirium. Her chief complaints were headache, dizziness, and visual impairment. Since recovery she has noticed a gradual change in vision. The eye grounds are negative at present. There was no history of insomnia or lethargy. Since the illness, she has complained of occasional pains in her arms.

Many interesting facts are suggested by the study of these cases. First, the family group is interesting and the diagnosis of a postencephalitic condition in the two sisters appears most probable. There is some question about the mother having had a similar illness. The fact that this developed following influenza is of interest in that we frequently have seen this relationship in other cases of encephalitis in children that we have studied.

The statements in the literature seem to show that encephalitis frequently develops after influenza, when the individual's resistance is lowered and he is most susceptible to a secondary invader, such as may be present in the etiologic agent of acute epidemic encephalitis. Cases of this type suggest the latter possibility and confirm the reports of others in this regard.

These two patients represent the only ones seen by us, in which encephalitis has occurred in two members of the family, from a large number of postencephalitic disturbances observed in the outpatient clinic and the neuropsychiatric wards. The question regarding the transmissibility of the virus causing encephalitis, must be considered in the above cases. Whether or not hospital isolation is essential will depend on further data. We do not practice isolation in our general hospital. No cases of hospital contagion have been reported in the literature with the exception of Wechsler, who reported two interns in the same hospital with encephalitis. We feel that direct trans-

mission in cases of encephalitis is almost negligible. Wechsler out of 864 cases found only five in which the disease occurred in two members of the same family. This constitutes 0.5 per cent. of the cases on which he has completed careful clinical statistical studies.

Two cases of acute epidemic encephalitis in children of the same family have been presented, with remarks concerning the question of contagion in these cases, and their relation to postinfluenzal conditions. The rarity of these instances suggests that they had better be considered as accidental, and that direct transmission in acute epidemic encephalitis, with the facts that we have at hand, may be considered as practically negligible.

DISCUSSION

Dr. William G. Spiller: It is very improbable that one child in this family caught the disease from the other within the interval of a few days between the two cases, but it is more than propable that both children were exposed to the same source of infection. I believe that the period in which epidemic encephalitis is more likely to be transmitted is before the correct diagnosis is made, when the micro-organism has not yet produced focal symptoms. I doubt whether it is likely to be transmitted after the symptoms of brain involvement are pronounced.

A CASE OF TUMOR OF THE FORAMEN MAGNUM, WITH EXHIBITION OF SPECIMEN. Dr. John H. W. Rhein.

This paper will be published in full in a later number of the Archives.

A CONTRIBUTION TO THE PATHOLOGY AND PATHOGENESIS OF UNILATERAL HYDROCEPHALUS. Dr. N. W. Winkelman and Dr. H. L. Eccles.

This paper will be published in full in a later number of the Archives.